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TULAREMIA

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CHICAGO

Among the few typically American diseases, tularemia takes high rank in reflecting well earned and deserved credit on the discoverers for personal self effacement and a truly scientific approach.

From a supposed letter to his sister written by a young boy visiting and hunting in California many years ago, in which it was said, among other things, "After one of my hunting trips, I have develepod 'rabbit fever,'" to the epoch-making publication of Pearse [1] (1911), who first described the clinical picture in cases in Utah, and McCoy [1a] (1911), who described "a plague-like disease of rodents, prevalent among the California rodents," the saga of this disease has been one of ever increasing importance. In 1912 McCoy and Chapin [2] discovered the causative organism and named it Bacterium tularense, in honor of Tulare County, Calif., where the disease was most prevalent. Wherry and Lamb [3] (1914) isolated the organism from a case of ophthalmic involvement in a man, and Francis [4] (1919) named the disease tularemia on account of finding the causative organism in the blood.

Tularemia occurs primarily in nature as a fatal bacteremia among wild rabbits, hares, sheep, cats, coyotes, dogs, foxes, hogs, muskrats, quails, sage hens, ground and tree squirrels, wild rats and mice. It may be transmitted from animal to animal by the rabbit louse (Haemodipsus ventricosus), rabbit tick, mouse louse, common bedbug (Cimex lectularius), deer fly (Chrysops discalis), horse fly or squirrel flea, or from animal to man by the bite of the deer fly or the wood tick (Derma-

1. Pearse, R. A.: Northwest Med. **3**:81, 1911.

1a. McCoy, G. W.: A Plague-Like Disease of Rodents, Hygienic Laboratory Bulletin 43, United States Treasury Department, Public Health Service, 1911.

2. McCoy, G. W., and Chapin, C. W.: Bacterium Tularense, the Cause of a Plague-Like Disease of Rodents, Hygienic Laboratory Bulletin 53, United States Treasury Department, Public Health Service, 1912, p. 17.

3. Wherry, W. B., and Lamb, B. H.: Discovery of the Bacterium Tularense in Wild Rabbits and the Danger of Its Transfer to Man, J. A. M. A. **63**:2041 (Dec. 5) 1914.

4. Francis, E.: Deer Fly Fever: A Disease of Man of Hitherto Unknown Etiology, Pub. Health Rep. **34**:2061-2062, 1919.

centor andersoni), from handling infected animals, from contact with infected flies and ticks or from the bites of various carrier animals.

This specific infectious disease is caused by Bacterium tularense, a small nonmotile gram-negative coccobacillus which grows only under aerobic conditions, especially on coagulated egg yolk and also on blood-dextrose-cystine agar. It stains in preparations under cover glass with ordinary aniline dyes, especially aniline gentian violet or crystal violet, and in sections with Mallory's eosin and methylene blue and notably with Gram's stain.

The distribution of the disease is widespread, from forty-six states and the District of Columbia to Japan (O'Hara's disease), Russia, Norway, Sweden, Austria, Canada and Czechoslavakia. Its extent in the lower animal kingdom is a matter of conjecture, but probably no other disease enjoys so wide a distribution.

CLINICAL TYPES

Tularemia in man manifests itself in several ways, such as a local cutaneous reaction, a conjunctivitis with regional adenopathy or a systemic infection. Francis [5] divided the various manifestations into the following types, depending on the portal of entry: ulceroglandular, pulmonary, meningeal, oculoglandular, glandular, typhoid and ingestive.

After an incubation period of one to ten days, with an average of three days, the infection manifests itself by an abrupt onset of headache, nausea, vomiting, chills, fever and generalized itching. The temperature shows an initial rise for two or three days, remission for one to three days and a secondary rise for one to three weeks. The temperature level is between 102 and 104 F. This is followed by weakness, loss of weight, prostration and drenching sweats.

With the ulceroglandular type a painful regional adenitis (fig. 1) follows the onset within forty-eight hours and precedes by twenty-four hours the local painful or painless papule (fig. 2) which appears at the site of entry. This papule soon breaks down, liberating a necrotic plug or core, and leaves an ulceration with ragged raised edges indolent in character, with a base of small fungating buds of granulation tissue. A generalized eruption consisting of macular, papular and pustular lesions may occur. The skin over the enlarged, painful and tender lymph glands is red, as is that over the subcutaneous lymphatic nodules and lymph channels extending from the focus of infection to the regional lymph glands. This manifestation resembles closely that of sporotrichosis.[6] The subcutaneous nodes and the epitrochlear and axillary

5. Francis, E.: Symptoms, Diagnosis and Pathology of Tularemia, J. A. M. A. **91**:1155 (Oct. 20) 1928.

6. Shelmire, B.: Tularemia Resembling Sporotrichosis: Report of Case, Arch. Dermat. & Syph. **19**:918 (June) 1929.

glands may or may not proceed to suppuration. Those which fail to suppurate remain hard, palpable and rather tender for several months. The blood count shows nothing remarkable excepting sometimes a mild leukocytosis.

The oculoglandular type has the following predominating characteristics: The conjunctiva is the portal of entry of the infecting material.

Fig. 1.—*A*, adenitis on the inner side of the elbow and primary lesion on the forefinger. *B*, axillary adenitis.

Fig. 2.—Multiple primary lesions.

The reaction consists of conjunctivitis associated with pain, swelling, edema and lacrimation, a papule on the conjunctiva of the lower lid and regional adenitis (submaxillary, anterior cervical, parotid, preauricular and sometimes the axillary group). Small discrete ulcers form on the conjunctivas. The general symptoms are the same as mentioned for the ulceroglandular type.

The pulmonary and meningeal forms show a dominant pneumonia, lobar or bronchial, or meningitis, usually in association with the ulceroglandular type, but pulmonary lesions are frequent in all types.

The predominating manifestations of the glandular types are: (1) absence of primary lesions and (2) glandular enlargement, especially the epitrochlear and axillary glands.

In the typhoid type, fever is the only remarkable symptom. The absence of primary lesions and adenitis adds to the difficulty of diagnosis. The general symptoms, which resemble closely those of typhoid fever, are usually severe.

The ingestive type, which may result from eating undercooked contaminated food or drinking contaminated water, has a symptom complex which resembles closely that of botulism. The symptoms include nausea, vomiting, abdominal pain and diarrhea, but there are also enlargement of the submaxillary and anterior cervical glands and sometimes conjunctivitis.

DIAGNOSIS

Francis [5] stated:

> Because tularemia was not borne in mind, the disease has been erroneously diagnosed as follows: 1. Clinicians have called it influenza, septic infection, typhoid fever and pneumonia. 2. Dermatologists have called it sporotrichosis on account of the subcutaneous nodules. 3. Pathologists have called it tuberculosis on account of the lesions in the lymph glands. 4. Serologists have called it undulant fever on account of the cross-agglutination of *Brucella melitensis* and *Brucella abortus*. . . .
>
> The clinician who bears in mind the following tetrad will seldom fail to diagnose a case of tularemia: (1) a history of having dressed or dissected a wild rabbit, or of being tick-bitten or fly-bitten; (2) a primary lesion of the skin in the form of a papule, followed by a persistent ulcer or a primary conjunctivitis, followed by ulcers of the conjunctiva; (3) persistent glandular enlargements in the region draining the primary lesion, and (4) fever of from two to three weeks' duration.
>
> Having recognized this tetrad in his patient, the clinician will prove his diagnosis (1) by obtaining an agglutination of *Bacterium tularense* by blood serum collected in the second week of illness and by noting an increase in the agglutinin titer in serum collected a few days later or in the third week, or (2) by isolation of *Bacterium tularense* from guinea pigs inoculated with material taken as early as the first week from the primary lesion or from the enlarged glands or the blood of the patient. Microscopic examination of cover-glass preparations taken direct from the patient is useless.

The agglutination phenomenon has certain notable features: 1. It is absent during the first week. 2. There is a constancy of agglutinins during the second week and a rise in titer during the following weeks, up to the seventh. 3. These agglutinins persist for many years, having been noted for twenty years after infection. 4. There is cross agglutination of Brucella abortus and Brucella melitensis. The titer of real

tularemia, i. e., that produced by B. tularense, is usually much higher than that produced by the other organisms. Immunity against future infection is specific.

The isolation of the organism must be made first by inoculation of guinea pigs with material from glands or conjunctiva or blood. Subcutaneous and intraperitoneal channels are employed. The animals should die within a week. From human beings positive cultures have been obtained from the blood only during the first week, from the third to the eighth day.

Foshay's intradermal test,[7] giving a specific cutaneous reaction, is of diagnostic value, especially in the first week, before the beginning

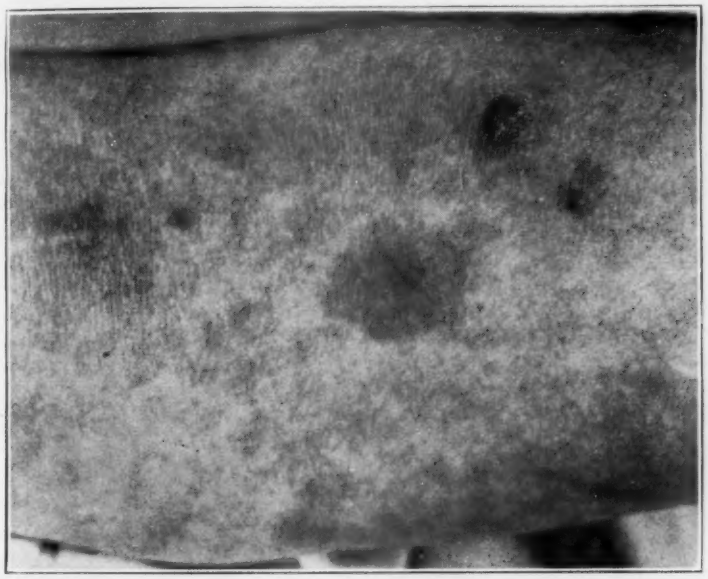

Fig. 3.—Three intracutaneous antigen reactions: left, twenty-four hours; center, one week; right, two weeks.

of agglutinin formation. An antiserum cutaneous test made with a suspension of detoxified Pasteurella tularensis organisms has been of value in only a very small percentage of cases.

ANTIGENIC REACTION

The first two weeks are most important in diagnosing the suspected disease, but it is also during this time that the most important diag-

7. Foshay, L.: Am. J. Clin. Path. **2**:7, 1932; Antiserum for Treatment of Tularemia, J. A. M. A. **101**:1447 (Nov. 4) 1933; Am. J. M. Sc. **187**:235, 1934. Simpson, W. M.: Ohio State M. J. **29**:35, 1933.

nostic procedure, the agglutination test, elicits negative reactions. I have therefore tried a measure which is hoped will fill this gap. Although only 10 cases have been studied, the method is being offered at this time as an incentive for some one more fortunately placed than I for unhampered clinical experimental work.

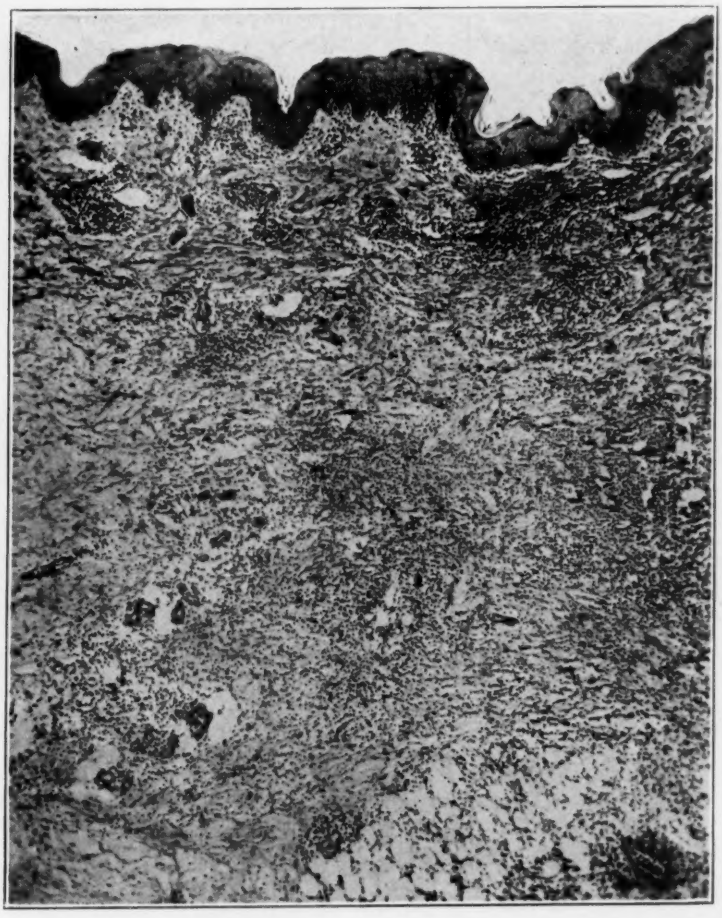

Fig. 4.—Histologic structure of the antigen reaction.

The procedure is as follows: The pus from an unopened gland is aspirated and divided into three equal portions. These separate portions are triturated with ten volumes of acetone, alcohol and 0.4 per cent saline solutions. The mixture is allowed to digest for twenty-four hours, with frequent agitation. The supernatant fluids are pipetted off and mixed. The alcohol and acetone are allowed to evaporate, and the original volume is made up with 0.4 per cent saline solution. The solu-

tion is sterilized on a water bath at 60 C. for two hours and twenty-four hours later for one hour. Tests for sterility are performed on agar plates. Phenol, 0.25 per cent, is then added.

As a test material, 0.1 cc. is introduced intradermally, and the reaction is read at the end of one-half hour (fig. 3). A large erythematous, edematous wheal with pseudopodia in some cases will result in a case of

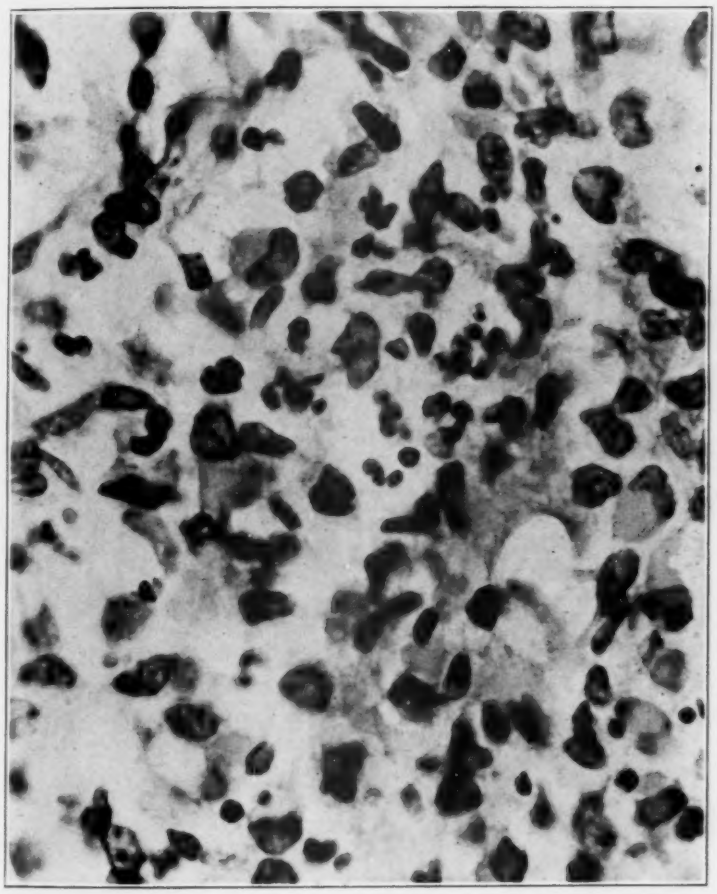

Fig. 5.—A section from figure 4 (× 1,000), showing the histiocytic response and the formation of a small abscess.

the disease. This reaction remains for twenty-four or more hours, depending on the severity of the condition. A control subject should show either no reaction or one that disappears in ten to fifteen minutes. In subjects presenting nonspecific reactions, the wheal disappears in from one to two hours. The earliest time at which a positive result was obtained was one day after onset of symptoms. Two weeks later a posi-

tive reaction was obtained with a tularemia agglutination test with a 1 : 1,280 dilution. The oldest condition was recognized five months after infection and had been diagnosed and treated as influenza, pneumonia and empyema.

This antigen also agglutinates the red blood cells of infected persons and produces a specific histiocytic response in the local tissues (figs. 4

Fig. 6.—Histologic structure of a primary lesion of the tuberculoid type.

and 5). Because of a true reticulocytic response in the local tissue, antibody stimulation was attributed to this antigen, and 2 patients were given no treatment other than this antigen. The glandular response was cessation in growth and focal necrosis, with suppuration of the large glands and gradual absorption of the smaller ones.

HISTOLOGIC STUDIES

Ulcers.—The histologic picture of tularemia is that of a specific granuloma. Francis [5] stated:

> Five, eight, thirteen and fourteen days after onset is the earliest that human tissue collected at autopsy has been sectioned. Lesions were found principally in the primary ulcer, lymph nodes, spleen, liver and lungs. *Bacterium tularense* has not been stained in sections of human lesions.

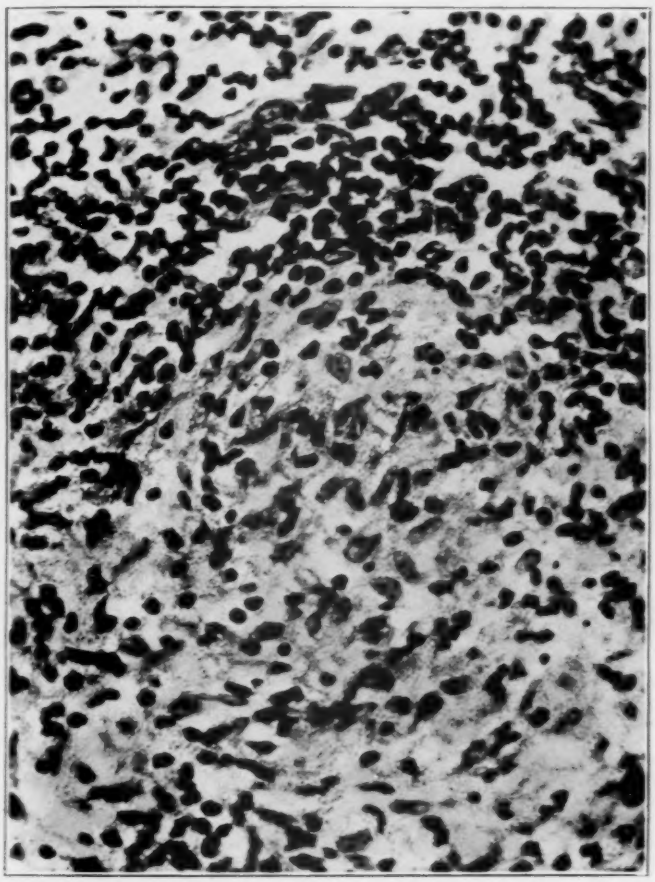

Fig. 7.—Tuberculoid arrangement in a primary ulceration.

The primary ulcer showed diffuse necrosis with nuclear fragmentation and infiltration with polymorphonuclear leukocytes, beneath which was infiltration with small lymphocytes.

The histologic changes in a late ulcer (figs. 6 and 7) present in 2 of the cases, are as follows: The section portrays the clinical appearance of the disease, i. e., dry and moist areas with verrucous-like pro-

jections from the base which are umbilicated. The epidermis as a whole is irregular. The stratum corneum is extremely hyperkeratotic, and many giant cells are present, especially in the plugs which fill an umbilication. Parakeratosis is notable. Hypergranulosis is present to a marked degree, in some areas as many as nine rows of cells in extent. The prickle cell layer is both acanthotic and edematous.

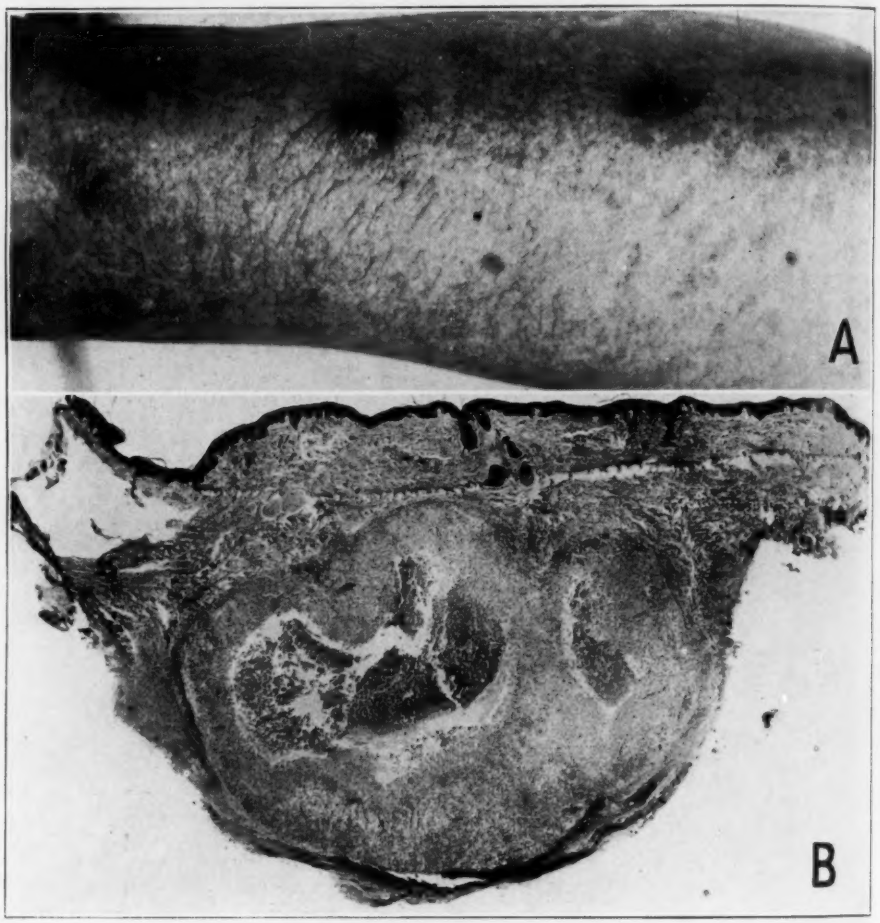

Fig. 8.—*A*, sporotrichoid arrangement of tularemic nodules on the arm. *B*, histologic view of a nodule shown in *A*.

The basal layer, though decidedly edematous, stains deeply and sharply. The interpapillary pegs are distinctly broadened excepting near an umbilication, where they spread out deeply and assume the form of bowed wrestler's arms in combat.

The corium is wholly disorganized. The pars papillaris is pale staining and edematous, especially the sub-basal zone. The interpapillary

pegs in many instances are separated from the corium by pools of fluid. The arterial, venous and lymphatic systems are widely dilated. The connective tissue is pale staining and edematous. The vacuolation is so great that it gives the appearance of a fine meshed sponge.

The cellular elements of the corium (fig. 7) are represented by perivascular and diffuse infiltration of small round cells, a noticeable

Fig. 9.—Histologic structure of a nodule shown in figure 8 *A* (high power).

increase in young and mature fibroblasts, histiocytes and many variably sized tuberculoid foci, consisting in some zones of a few leukocytes and many epithelioid cells and in others of areas of necrosing and degenerating connective tissue with proliferation of epithelioid cells. These are walled in by myriads of lymphoid cells interspread with connective tissue cells and few epithelioid cells. Here and there a few plasma and leukocytic cells may be seen (fig. 7). A slight increase in the number

of eosinophilic cells normally seen is present. The elastic fibers are fragmented.

The nerve structures seen show no organic changes. The sweat glands are dilated and in some areas are undergoing degeneration, probably due to internal pressure.

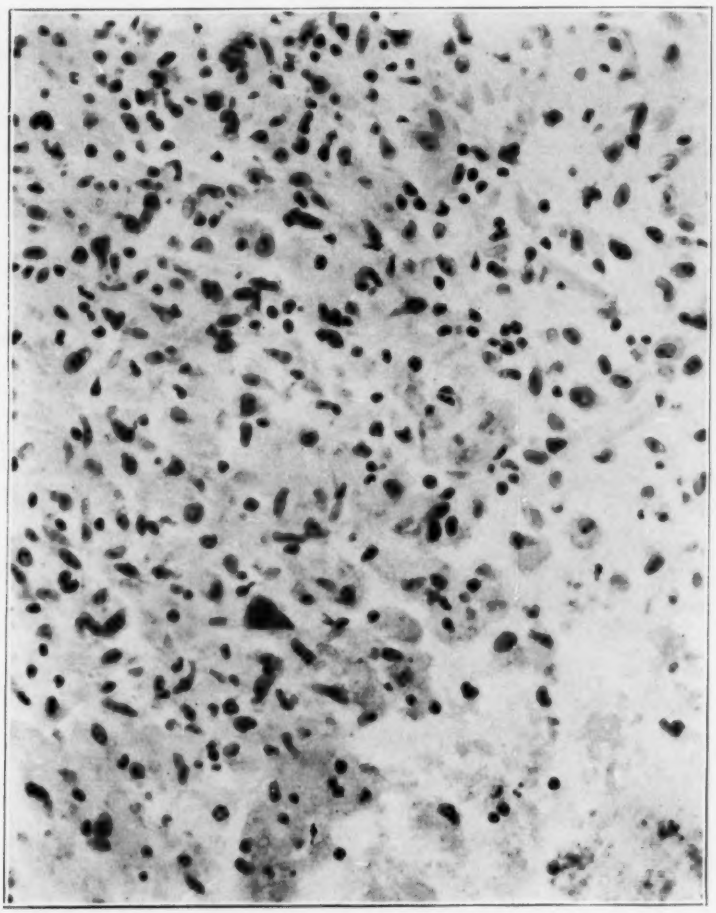

Fig. 10.—An area from figure 9 highly magnified. The histiocytes and fibrioblasts are easily recognized.

Lymph Node.—The histologic picture of the lymphatic nodules (figs. 8, 9 and 10) is as follows: Deep in the corium and extending into the subcutaneous tissue lies a large inflammatory nodule, the central portion of which shows colliquative necrosis; cellular debris enmeshed in a basophic granular stroma is present. Histiocytes, lymphoid cells and a few connective tissue cells are scattered throughout this mass; surround-

ing this pus pocket is a zone of pale-staining large vesicular nucleated cells (histiocytes), the protoplasmic portion of which is foamy. In some many inclusion bodies may be seen. A few small lymphoid cells are present. The next zone is composed principally of histiocytes, a moderate number of fibroblasts and small lymphoid cells. Here and there a large multinucleated giant cell may be seen. The outer zone is a very dense mixture of small lymphoid cells, plasma cells (many of the double-nucleated variety), fibroblasts and histiocytes. A firm, compressed band of connective tissue encircles the mass. Between these focal infiltrates and the epidermis the perilymphatic spaces and the lymphatic vessels are widely dilated, and a pronounced perivascular and perilymphatic infiltrate consisting of lymphoid cells and histiocytes, both of the wandering and of the fixed type, are present. With the exception of widely dilated and edematous spaces at the epidermodermal junction and some slight generalized edema, the epidermis appears normal.

Site of Antigenic Reaction.—An interesting phenomenon is the comparison of the histiologic response of the tissue to the bacillary invasion with that to the dermal antigen injection. The histologic reaction to the antigen is as follows (figs. 4 and 5): The epidermis is edematous with many wandering leukocytes. The corium shows massive edema. The involved connective tissue areas present a small cell, sponge rubber appearance, i. e. are vacuolated. The cellular infiltrate is massive and extends from the epidermis to and into the subcutaneous tissue. The lymphatic and vascular systems are dilated and show decided cellular infiltrate consisting of young histiocytes, both of the wandering and fixed cell types, and a few small lymphoid cells. Scattered throughout the infiltrated area small abscesses are seen.

It is observed that, whether from the bacterial or antigenic stimulation, the response is reticuloendothelial.

TREATMENT

The treatment of this condition was purely symptomatic until the discovery of Foshay's serum,[7] which is given intravenously in 15 to 30 cc. doses on two consecutive days. Elson recommended highly 25 drops of syrup of ferrous iodide U. S. P. taken internally in one-half glass of water and compresses wet with the following solution applied on the glands:

Tincture of opium..... 1 oz. (30 cc.)
Solution of lead subacetate.....to make 3 oz. (90 cc.)
M. Sig.: 1 drachm (4 cc.) to 8 ounces (240 cc.) of water. Apply every four hours.

Alternate these compresses with compresses wet with a weak solution of sodium bicarbonate or calcium hypochlorite. Powers and Powers recommended the combined use of sulfanilamide and antiserum. Neo-

arsphenamine and irradiation have their advocates. Sulfathiazole and sulfamethylthiazole have been tried, with some encouragement from their advocates. A report will follow on the very promising value of the tularemia antigen as a therapeutic agent.

SUMMARY

1. A résumé of the historical, clinical and diagnostic measures for the identification of a tularemic infection is given.

2. An antigen made from necrosing glands is offered as an aid to the early diagnosis.

3. Descriptions of the histologic pictures of an early ulcer, a subacute ulcer, a lymphatic gland and the site of an antigen reaction are given.

4. A review of the treatment is given.

Miss Bertha Culka gave technical assistance.

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XCII. HISTOLOGY OF NEURODERMATITIS

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In a preliminary report Engman and MacCardle [1] described briefly a decided reduction in the magnesium content of the skin of patients with chronic disseminated neurodermatitis. The fact that all the patients with a clinical diagnosis of chronic disseminated neurodermatitis showed this deficiency whereas there was no decrease in magnesium in patients with other inflammatory lesions of the skin strongly suggests that this type of neurodermatitis is a disease entity recognizable both clinically and chemically. The purpose of this study is not only to ascertain whether neurodermatitis is a histologic entity but also to present in detail the histologic features observed in 33 cases of chronic disseminated neurodermatitis in order to provide an accurate basis of comparison for a subsequent description of the minerals in ashed sections of skin from the same patients.

The basic factors concerned in the development of chronic disseminated neurodermatitis are unknown. Fifty years ago Brocq [2] made a histologic study of this disease and suggested that it was of nervous origin, the surface pruritus and the epidermal thickening being the

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Studies, observations and reports from the Department of Dermatology of the Barnard Free Skin and Cancer Hospital and the Anatomical Laboratory of Washington University School of Medicine.

Dr. E. V. Cowdry gave assistance and advice, and Dr. Roy L. Kile and Dr. Paul J. Catinella gave clinical assistance.

1. Engman, M. F., and MacCardle, R. C.: A Histochemical Study of Neurodermatitis: Preliminary Report; Microincineration and Spectrographic Analysis, Arch. Dermat. & Syph. **42**:109 (July) 1940.

2. Brocq, L.: Névrodermite aiguë diffuse chez une malade atteinte de plaque de névrodermite circonscrite chronique de la paume des mains, Ann. de dermat. et syph. **2**:397, 1891.

initial changes. Later Vignolo-Lutati [3] described a perineural edema, but this has not been confirmed. Alexander [4] and Gans,[5] who confirmed Alexander's earlier work, stated the belief, because of the perivascular infiltration, that the primary reaction is centered around the blood vessels in the cutis and the epidermal changes are secondary. Brocq and Jacquet [6] described edema around the lymphatic channels with multiplication of the endothelial cells of the lymph vessels and a perilymphatic infiltration of lymphocytes which subsequently involved the blood vessels of the papillae. Becker [7] and Stokes [8] agreed that there is a neurocirculatory instability.

Bukovsky [9] expressed the opinion that before the onset of cutaneous lesions in neurodermatitis, a toxic substance in the blood acts on the peripheral nerve terminals causing pruritus, dilatation of the blood vessels and edema. Bukovsky's concept was based on a careful study of the histologic changes in neurodermatitis, although he presented no evidence of actual damage to peripheral nerve endings. Dind [10] did not agree with this interpretation of the histologic changes. Wise [11] strongly advocated Bukovsky's views and stated that neurodermatitis "possesses peculiar clinical and histological characteristics." Alexander [12] described neurodermatitis as a definite clinical entity that is characterized by decided edema without the formation of epidermal vesicles, dissolution of pigment from basal cells in active lesions that are surrounded by hyperpigmented areas of epidermis and invasion of the epidermis by wandering cells (leukocytes?) emanating from dermal

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3. Vignolo-Lutati, K.: Neurodermatitis linearis psoriasiformis, Arch. f. Dermat. u. Syph. **111**:747, 1912.

4. Alexander, A.: Neurodermatitis, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 6, p. 371

5. Gans, O.: Die Prurigogruppe, in Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, p. 242.

6. Brocq, L., and Jacquet, L.: Notes pour servir de l'histoire des névrodermites: Du lichen circumscriptus des anciens auteurs ou lichen simplex chronique de M. le Dr. E. Vidal, Ann. de dermat. et syph. **2**:193, 1891.

7. Becker, S. W.: Dermatoses Associated with Neurocirculatory Instability, Arch. Dermat. & Syph. **25**:655 (April) 1932.

8. Stokes, J. H.: Functional Neuroses as Complications of Organic Disease, J. A. M. A. **105**:1007 (Sept. 28) 1935.

9. Bukovsky, J.: Zur Frage der Neurodermatiden, Česka dermat. **3**:57, 1922.

10. Dind, M.: Essai sur les lichens; la lichénification, Ann. de dermat. et syph. **6**:273, 1920.

11. Wise, F.: Pruritus with Lichenification, New York M. J. **118**:688, 1923.

12. Alexander, A.: Zur Histologie des Lichen chronicus Vidal, Dermat. Ztschr. **33**:251, 1921.

papillae. However, he left unanswered the question of neurodermatitis as an anatomic entity.

Brunsting,[13] in his excellent analysis of the precipitating factors in neurodermatitis, stated that while the instability of the vasmotor system may be a contributory factor, "it is subordinate and probably secondary to a background of a specific hypersensitivity," and he and Sulzberger, Spain, Sammis and Shahon [14] therefore designated this disorder "atopic dermatitis." The association of cataract with neurodermatitis [13] is interesting, because the lens is an epidermal tissue and because cataract is so frequently concomitant with mineral disturbances, such as tetany.

MATERIAL AND METHODS

Biopsy specimens of skin of 33 patients with chronic disseminated neurodermatitis were taken mostly from the cubital fossa and popliteal regions, where active lesions prevailed, and in 22 of the cases specimens were also removed from the thoracic region of the midaxillary line, where the skin had never been affected by detectable lesions. Sites for the taking of biopsy specimens from diseased patients were treated with a 3 per cent mixture of boric acid in cold cream alone for one week previous to the time of biopsy, in order to cleanse the lesions from contaminant substances. The specimens were cut from the centers of large alcohol-washed areas that were anesthetized by a 0.5 per cent aqueous solution of procaine hydrochloride injected intradermally in the surrounding skin about 30 mm. distant from the cut (block anesthesia). Excised specimens of skin from patients under general anesthesia do not differ histologically from those taken during local anesthesia when the latter are removed immediately after injection of the procaine hydrochloride. However, if there is a delay it is possible that perivascular infiltrations may develop, as we have observed in rats even ten minutes after injection.

Small portions of each biopsy specimen were fixed in dehydrated alcohol and solution of formaldehyde (9 cc. of dehydrated alcohol plus 1 cc. of 40 per cent solution of formaldehyde), Bouin's and Regaud's fluids and Zenker's solution prepared with solution of formaldehyde. Paraffin sections 5 and 6 microns thick of this fixed material were stained with Masson's [15] trichrome stain and with ordinary hematoxylin and eosin. A section of normal and one of diseased tissue were mounted on the same slide in most instances to make the comparison more direct. An ocular micrometer was employed in the measurements, but the intensity of staining was estimated visually. Portions of the same specimens were studied by microincineration and spectrographic analysis, a preliminary report of which has been published.[1]

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13. Brunsting, L. A.: Atopic Dermatitis (Disseminated Neurodermatitis) in Young Adults, Arch. Dermat. & Syph. **34**:935 (Dec.) 1936.

14. Sulzberger, M. B.; Spain, W. C.; Sammis, F., and Shahon, H. I.: Studies in Hypersensitiveness in Certain Dermatoses: I. Neurodermatitis, J. Allergy **3**: 423, 1932.

15. Masson, P.: Carcinoids and Nerve Hyperplasia of the Appendicular Mucosa, Am. J. Path. **4**:181, 1928.

The regional distribution of the normal and pathologic biopsy specimens and the age distribution of the patients are given in the following tabulation:

Normal skin, total number of patients		83
Regional distribution		
Cubital fossa	18	
Popliteal spaces	27	
Neck	5	
Back	10	
Abdomen	11	
Head and face	6	
Foot	1	
Hand	2	
Chest	3	
Distribution according to age of patient		
Birth to 10 years	12	
11 to 20 years	24	
21 to 30 years	9	
31 to 40 years	21	
41 to 50 years	4	
51 to 60 years	2	
61 to 70 years	5	
71 to 80 years	4	
81 to 90 years	1	
91 to 100 years	1	
Neurodermatitis skin, total number of patients		33
Regional distribution of specimens		
Active lesions	33	
Cubital fossa	21	
Neck	3	
Popliteal spaces	10	
Unaffected skin	22	
Midaxillary line	22	
Healed lesions	6	
Cubital fossa	4	
Neck	2	
Distribution according to age of patient		
Birth to 10 years	7	
11 to 21 years	11	
21 to 30 years	6	
31 to 40 years	4	
41 to 50 years	0	
51 to 60 years	0	
61 to 70 years	1	
Other cutaneous diseases, total number of patients		55
Psoriasis	13	
Chronic dermatitis	9	
Lichen planus	2	
Contact dermatitis	8	
Exfoliative dermatitis	5	
Xeroderma pigmentosum	2	
Senile keratosis	1	
Pemphigus	5	
Infantile eczema	1	
Nummular eczema	1	
Erythema multiforme bullosum	1	
Ichthyosis	1	
Lichen simplex chronicus	6	

ACTIVE NEURODERMATITIC LESIONS.

Epidermis.—The corneum in disseminated neurodermatitis is generally about eight to ten times thicker than the normal corneum (table), and the keratin deposits are more intensely stained with the ponceau xylidine of Masson's trichrome method, but not with hematoxylin and eosin. Under areas of hyperkeratinization, the keratohyalin granules in the stratum granulosum are large and occupy almost the entire cytoplasm. Occasionally small areas of parakeratosis may be found under which the granular cells contain vacuolated keratohyalin granules (fig. 1), although sometimes there is no evidence of keratohyalin gran-

ules under such areas. Within a single area parakeratotic and hyperkeratotic processes may alternate with one another, for the corneum is frequently stratified with alternating layers of dekeratinized cells and hyperkeratinized cells. This stratification of the corneum is well differ-

Fig. 1.—Section of active neurodermatitic lesion (Zenker's solution prepared with solution of formaldehyde; Masson's trichrome stain; × 945), showing vacuoles in cells of stratum granulosum, absence of keratohyalin granules and perivacuolar membrane stained with ponceau xylidine.

entiated by the use of Masson's trichrome method of staining sections fixed in Zenker solution prepared with solution of formaldehyde (fig. 2).

It is pertinent here to note that in areas of parakeratosis where the layer immediately adjacent to the stratum granulosum is nonkeratinized

(indicating that parakeratosis was the process occurring at the time of biopsy), there is no pigment in the basal cells, and the intercellular fibrils are not heavily keratinized (that is to say, they are not heavily stained with ponceau xylidine, which is taken up readily by keratin but not by much else in sections of skin). However, neither is there any evidence of pigment in areas of hyperkeratosis, but the intercellular fibrils are heavily keratinized and thickened even between the basal cells. Under corneal areas that are stratified with hyperkeratotic and parakeratotic layers of cells, with the layer adjacent to the stratum granulosum heavily keratinized (indicating that hyperkeratosis was the process occurring at the time of biopsy), the intercellular fibrils are also heavily keratinized (fig. 2) and the basal cells pigmentless. Under regions of

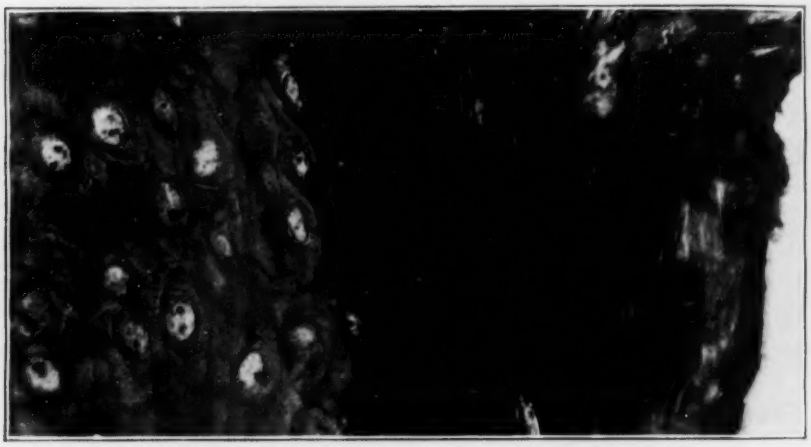

Fig. 2.—Section of active neurodermatitic lesion (Zenker's solution prepared with solution of formaldehyde; Masson's trichrome stain; × 520), showing stratification of parakeratotic-hyperkeratotic corneum.

hyperkeratosis the basal layer of the epidermis may or may not be thickly beset with clear cells that seem to be invading the epidermis from the cutis, while under areas of parakeratosis these cells are absent. The relation of these clear cells to pigmentation and keratinization will be discussed in another part of the paper.

A stratum granulosum is always present in the skin of patients with neurodermatitis, although it may lack keratohyalin granules in the localized spots where parakeratosis was evidently in progress at the time the biopsy specimen was taken. In such parakeratotic areas the stratum granulosum cells can be recognized by their flatness, by the lack of intercellular fibrils and by the staining of their homogeneous-looking cytoplasm with aniline blue in Masson preparations. These localized

spots of parakeratosis are of relatively infrequent occurrence in active lesions and are about 80 to 100 microns in diameter

The spinous cells of the epidermis in neurodermatitis are twice the size of normal cells (table). This increase in size would lead the observer to believe that the cellular hypertrophy is accompanied by an imbibition of water. However, there are rarely any vacuoles present in the cytoplasm, except in localized groups of cells that possess large perinuclear vacuoles (*altération cavitaire*). The cytoplasm of the distal spinous cells is usually deeply colored with aniline blue, while that of the cells nearest the basal layer is colored faintly with acid fuchsin. It

Average Measurements of Components of Normal and Pathologic Human Skin*

Structure	Normal Skin	Neurodermatitis			Infantile Eczema	Exfoliative Dermatitis	Contact Dermatitis	Psoriasis
		Active Lesion	Unaffected	Healed Lesion				
Corneum, thickness.....	10	150	80	150	200	350	100	150
Stratum granulosum, thickness.....	8	25	6	20	38	70	...	...
Epidermis, interpeg thickness.....	40	125	80	150	...	450	80	...
Rete peg, length.....	30	400	80	450	600	...	250	375
Rete peg, apical width...	8	105	18	75	...	...	...	470
Fibrils, thickness.....	—0.5	1.0+	—1.0	1.0+	...	...	...	...
Intercellular canals, width.....	0.5	2.0	—1.0	1.5	...	...	...	...
Spinous cell, size.....	8×16	14×25	10×15	15×20	...	...	...	...
Spinous nuclei, size.....	5×5	7×8	5×6	7×7	...	...	...	...
Basal cell, size.....	5×15	8×20	6×20	7×21	...	...	...	...
Blood vessel, diameter..	5.5	30	6	32	...	...	...	40
Perivascular infiltration collar, thickness.....	5.0	40	20	20	...	...	...	...
Perivascular infiltration collar, length.....	5.0	300	100	200	...	...	...	...

* These figures were obtained by calculating the average measurements for 62 specimens of normal skin and 33 specimens of neurodermatitis skin from patients of the same age groups. The other cutaneous diseases are discussed in the text. All measurements are expressed in microns.

seems that these distal spinous cells, especially those nearest the corneum, are distended with some highly viscous coagulated product, such as protein, of a homogeneous consistency.

The intercellular fibrils of the spinous cells are thicker than normal fibrils (table) and they are heavily stained with ponceau xylidine under areas of hyperkeratosis. The walls of these cells are clearly discernible, being stained with acid fuchsin, which differentiates them from the fibrillar basket that is colored with ponceau xylidine. In normal spinous cells the walls are not clearly differentiated; the whole epidermis seems to be a basket of fibrils in which packets of protoplasm (spinous cells) are dispersed.

The nuclei of all spinous cells in neurodermatitis skin are larger than those of normal spinous cells (table), and they are much less

intensely colored with acid fuchsin. The chromatin is thinned, and the nucleoli are more numerous in the spinous cells nearest the basal cells. Usually all of the nucleoli are heavily stained with ponceau xylidine in neurodermatitis spinous cells, whereas in cells of normal skin only one nucleolus is colored intensely with acid fuchsin and the remaining ones are only faintly colored. In hematoxylin-eosin preparations, the nucleoli of neurodermatitis spinous cells are all faintly stained with hematoxylin, while only one nucleolus of a normal cell is heavily stained and the remaining ones are faintly colored. From the foregoing observations, it appears that in neurodermatitis skin the nuclei of the spinous cells not only are much more fluid in consistency but also possess nucleoli that are composed of some abnormal substance (probably akin to keratin, since it stains so heavily with ponceau xylidine). If staining with hematoxylin is indicative of normal chromatin, then these nucleoli are not composed of normal chromatin.

Intercellular edema is apparent everywhere in the spinous cell region of neurodermatitis skin. The intercellular canals are generally three to four times greater in diameter than in normal skin (table). In active lesions these canals seem to stretch so much that offshoots in the form of small buds are evaginated from the main channel, evidently to compensate for the pressure of excess intercellular fluid (fig. 3). These buds resemble the empty sheath buds that appear in nerve fibers in Recklinghausen's disease, although the canal buds in neurodermatitis are probably not permanent growths but merely temporary bulges in the channel wall at places that are not well reenforced. The canals are apparently distended with a clear fluid, for there is no evidence of any stainable material within them. The walls of these intercellular canals are clearly visible, especially so in the proximal region of the spinous cell layer. In very active lesions it seems that these canals have imbibed so much fluid that their dermal surfaces are distended into large bulbs which probably explode in extreme edema (fig. 3). The canals of normal skin do not possess clearly visible walls, and they begin as poorly demarcated spaces in the cutis immediately beneath the basal cells. It is possible that dermal bulbs that distend into the collagenic fibers in neurodermatitis skin do not represent the real beginnings of the intercellular canals, for there are many other free dermal spaces that open into intercellular spaces without any delimiting membranes.

Mitotic figures are not numerous and are frequently not seen in the epidermis of active lesions. When they do occur they are confined largely to the basal cells and the spinous cells immediately adjacent to them in the elongated rete pegs. Dividing cells are usually clear, their cytoplasm being stained only faintly with acid fuchsin. It is difficult to distinguish mitotically dividing cells in the epidermis from certain clear cells in the basal layer

Circumscribed areas of vacuolated perinuclear cytoplasm are not infrequently encountered in the spinous layer of skin from active neurodermatitic lesions. This, however, is not true of unaffected neurodermatitis skin. In sharply delimited areas of epidermis the nuclei of the

Fig. 3.—Section of active neurodermatitic lesion (alcohol-formaldehyde solution; Masson's trichrome stain; × 785), showing a large bulb on intercellular canal extending in the cutis and blind offshoots from the sides of other canals within epidermis.

proximal spinous cells may possess large perinuclear vacuoles. These vacuoles may be arranged in different ways, appearing sometimes as large circumnuclear vacuoles and sometimes as polar vacuoles placed symmetrically at either pole of the nucleus. These polar vacuoles, there-

fore, may be called distal polar vacuoles or proximal polar vacuoles (fig. 4). The vacuolated areas are usually about 200 microns in width. Occasionally they involve the basal cells. French writers have designated this condition *altération cavitaire*. Such areas in our specimens are not related to parakeratosis or to pigmentation. The cutis beneath them is no more edematous than is the cutis in other places where no perinuclear vacuoles appear. The nuclei of such vacuolated cells are always invaginated by pressure of the vacuoles, giving the appearance of pyknotic nuclei; however, the staining capacity of the nuclear contents does not differ from that of other noninvaginated nuclei.

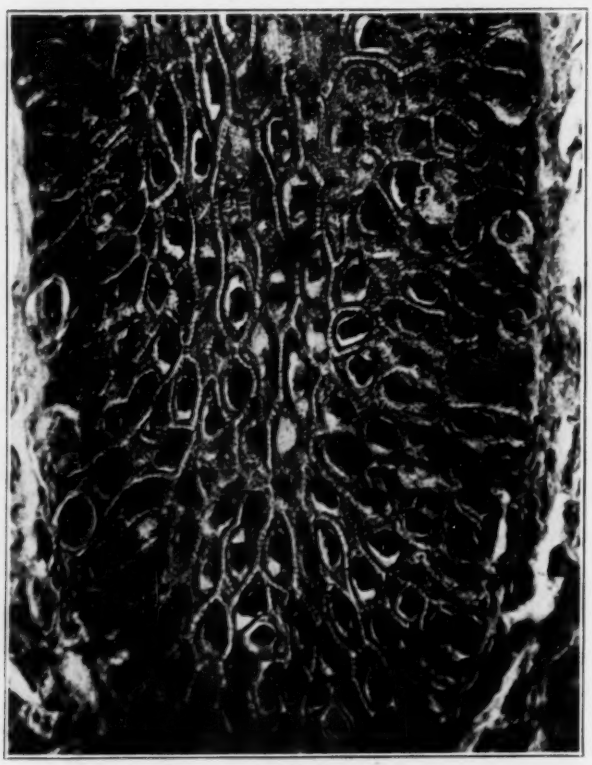

Fig. 4.—Section of active neurodermatitic lesion (alcohol-formaldehyde solution; Masson's trichrome stain; × 520), showing perinuclear vacuoles in spinous cells immediately above basal layer and intense staining of basal cells.

The basal cells of neurodermatitis skin are not usually any larger than those of normal skin, and their staining capacity is not much different except that the nucleoli are all heavily colored with ponceau xylidine, indicating, as in the nucleoli of the spinous cells, that their chemical or physical constitution has been altered. In hematoxylin-eosin–stained preparations these nucleoli are faintly colored with hematoxylin,

there being only occasional nucleoli which are heavily stained with hematoxylin. In normal basal cells the nucleoli are lightly stained with ponceau xylidine in Masson preparations, and at least one of them in every cell is heavily stained with hematoxylin in hematoxylin-eosin preparations. The nucleus as a whole appears normal in other respects.

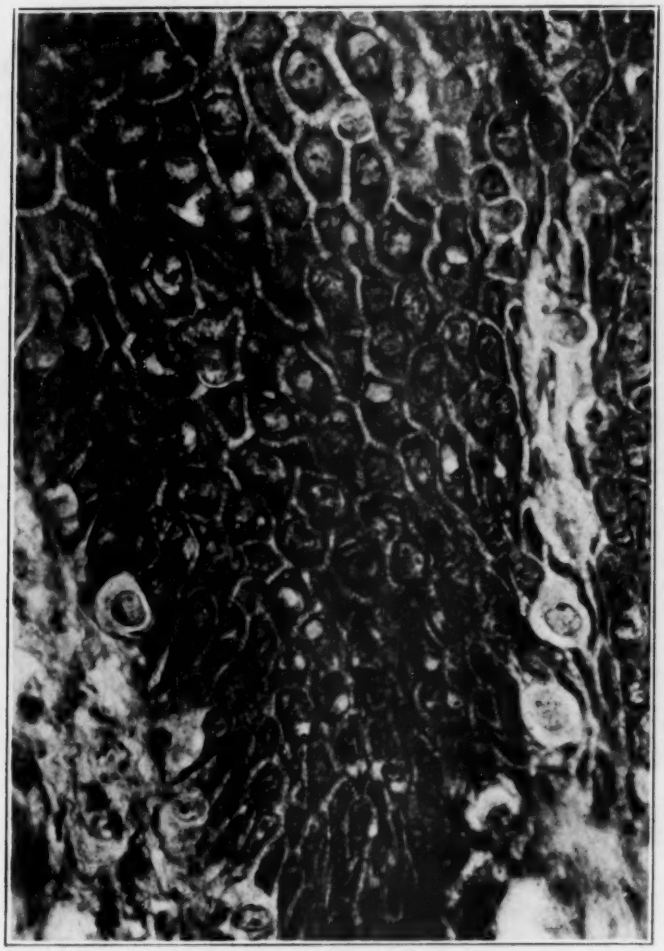

Fig. 5.—Section of active neurodermatitic lesion (alcohol-formaldehyde solution; Masson's trichrome stain; × 520), showing clear cells in the basal layer.

No melanin was seen in the basal layer of any active neurodermatitic lesion.

The basal layer of the epidermis of neurodermatitis skin is sometimes apparently invaded by a large number of clear cells that resemble monocytes (fig. 5). There are always many clear cells in areas where the basal layer is beginning to disintegrate in an active lesion, and

there may or may not be clear cells under areas of pronounced hyperkeratosis. These clear cells are always absent beneath areas of parakeratosis where no keratin was being deposited in the corneum at the time the specimen was taken for biopsy. In no active lesions have we found any pigment associated with the presence of clear cells. On the other hand, pigment is absent in the many areas where the clear cells are also absent.

Such clear cells may be seen also in normal skin, although they are much smaller and of different cytoplasmic structure than the clear cells of neurodermatitis skin. A clear cell from normal skin is only about 8 by 10 microns in size, while one from neurodermatitis skin is always at least 20 by 20 microns.

The cytoplasm of a clear cell in normal skin is not homogeneously clear. It consists of a small cytosome surrounding a small, crescent-shaped, deeply stained nucleus. From this peripherally located mass of nucleated cytoplasm extend fine strands of cytoplasm to the opposite peripheral cell wall. These strands evidently pass between large and small cytoplasmic vacuoles, which not only fill the cytoplasm but also invaginate the nucleus. The bodies of such cells rarely protrude into the cutis but seem to be tightly bound between basal cells.

The clear cell of neurodermatitis has a homogeneous-looking cytoplasm except for a few finely dispersed particles stainable with acid fuchsin. There are no vacuoles or cytoplasmic strands. The faintly stained nucleus is larger than that in the clear cell of normal skin and is centrally located.

The rounded portions of the cytosomes of neurodermatitis clear cells seem to protrude into the cutis, while relatively thin cytoplasmic "pseudopodia" of their epidermal surfaces extend into the interspaces between the heavily stained basal cells. Such a topographic arrangement conveys the impression that these cells are "invading" the basal layer. Furthermore, clear cells appear occasionally in the middle of the spinous layer. It may well be that such cells are not invading the epidermis from the cutis at all but are migrating from the epidermis to the cutis. There is no good evidence to prove either contention. On the other hand, the protruding cytosomes of the clear cells of the basal layer may simply represent the bulging of enlarging clear cells that were already resident in the epidermis—the protrusion being a factor in compensating for additional pressure.

However, in active neurodermatitic lesions in which the epidermis is highly edematous and the basal layer "frayed," a condition apparently just preceding the complete breakdown of the epithelium, clear cells are numerous in the basal layer and show many different degrees of protrusion. Some have only a small surface extending into the basal layer, while others have larger portions in the basal layer. Also there are

many clear cells found in the papilla beneath the epidermis which resemble closely the clear cells of the basal layer.

The fact that these clear cells have no spinous processes also indicates that they are not true epidermal cells but cells from some other part of the skin. In neurodermatitis, at least, these clear cells of the basal layer may be derived either from white blood cells or from connective tissue elements which invade the epidermis.

Cutis.—In disseminated neurodermatitis the morphologic changes in the cutis are neither specific in fundamental nature nor particularly pronounced in degree, as compared with the variety of changes in the epidermis. In active lesions in which the epidermis is thinned and broken over the edematous surface of an expanded papilla, the collagenic fibers are thick and tightly bound around the rete pegs but thinner and more loosely bound at the epidermal surfaces of the papillae. In every case of neurodermatitis we have noticed perivascular infiltrations of lymphocytes (table) in which fibroblasts are numerous, although in most instances the infiltrations are not widespread. It is only beneath areas where the epidermis is breaking down over an edematous papilla that extensive perivascular infiltration occurs. In view of Alexander's [4] contention that the blood vascular system is the primary shock tissue in neurodermatitis, it is pertinent to note that even beneath the most acanthotic epidermis perivascular infiltration is seldom more evident than in some areas of apparently normal skin (table). However, the blood vessels were dilated in every one of our 33 cases, regardless of the perivascular infiltration (table).

The extent of perivascular infiltration is difficult to describe in comparing one section with another. We have therefore made measurements in a few specimens of typical neurodermatitis skin and in other specimens of skin to determine not only the approximate circumference, in microns, of the collar of extravasated blood cells around certain blood vessels but also the length of sector of the vessel along which the infiltrative collar extends. These measurements are recorded in the table.

In active lesions there is no instance of a dense perivascular infiltrative collar in the papillae, although there are many in the subpapillary cutis. Such collars vary in size, but even the smallest one is as large as any perivascular infiltration in normal skin. The largest ones are usually five to ten times greater in length in neurodermatitis skin than in normal skin and about three to four times thicker. In some active lesions none of the many perivascular infiltrations is larger than the few which occur in normal skin. However, in the majority of active neurodermatitic lesions perivascular infiltrations far surpass those in normal skin both in size and in number.

In unaffected neurodermatitis skin the subpapillary perivascular infiltrations are usually of the same magnitude of size as are those of

active lesions (table), but they are not nearly so numerous. There are usually no perivascular infiltrations in the dermal papillae, although in unaffected skin, as well as in active lesions, there are usually many wandering, isolated white blood cells and connective tissue cells to be found in these bodies.

Although perivascular infiltrations are of no less extent in number in healed lesions than in active lesions, the circumference and length of the masses of cells in healed lesions are usually about one half as great as in active lesions.

These observations seem to indicate not only that perivascular infiltration in normal skin is much more common than is commonly believed but also that in some highly active neurodermatitic lesions the development of perivascular infiltration evidently lagged far behind the rapid changes in the epidermis.

In the expanded edematous papillae there are many wandering cells that closely resemble monocytes and fibroblasts. In such areas the clear cells that stud the basal layer are similar to monocytes. In a few instances the wandering monocytes contain granules of a greenish brown pigment which may be shown by incineration to contain iron (hence, probably not melanin). In the deeper part of the cutis there are a few chromatophores containing melanin.

UNAFFECTED NEURODERMATITIS SKIN

Specimens of unaffected neurodermatitis skin were obtained from the thoracic region of the midaxillary line of patients who had cubital lesions at the time of removal of tissue for biopsy. Lesions had never occurred in the region of the midaxillary line in these patients, and they rarely occur there.

Epidermis.—The corneum of unaffected neurodermatitis skin is considerably thicker than that of normal skin (table). The whole epidermis is also thicker. There is not much evidence of parakeratosis, and there are no places where the stratum granulosum is free from granules of keratohyalin. The intercellular fibrils are more heavily colored than those of normal skin (stained on the same slide), but they are not any thicker than normal ones.

The spinous cells are a little larger than average spinous cells of normal skin from healthy persons. The distal and proximal ones stain alike with acid fuchsin as in normal skin. There are no intracellular vacuoles. The nuclei, although larger than in normal cells, take the dye in much the same way as normal nuclei. The nucleoli stain faintly with ponceau xylidine in Masson preparations, and one or two of them stain heavily with hematoxylin in hematoxylin-eosin preparations, as do those of normal cells.

The basal cells contain large amounts of melanin deposited in the cytoplasm distal to the nucleus (fig. 6). This is not true of all parts of the basal layer, where many cells contain no detectable pigment. These cells are no wider than those in the skin of normal persons, but they are invariably longer than basal cells in the skin of normal persons of the same age (table).

The basal layer contains many clear cells. The clear cells are not restricted to areas of hyperpigmentation but are equally numerous in nonpigmented areas. The nature of such cells is not known, but they do not seem to be related to keratinization or to pigmentation.

Fig. 6.—Section of unaffected skin from the midaxillary line of a patient with neurodermatitis (alcohol-formaldehyde solution; Masson's trichrome stain; × 520), showing acanthotic epidermis and hyperpigmentation of some basal cells, clear cells and mitotic figure in the spinous layer.

The hyperpigmentation of the skin of patients with neurodermatitis is probably an important factor in the development of a lesion. The basal cells probably become so overloaded with melanin that when the limit of pigment tolerance is reached, they suddenly release pigment components, such as free sulfur, that are injurious to the rest of the epidermis and that induce hyperkeratinization.

Cutis.—The cutis is tightly bound to the rete pegs by thick collagenic fibers. The blood vessels are of normal caliber, and there is

not as much perivascular infiltration as in active lesions (table). In the dermal papillae, however, the collagenic fibers are thin and loosely bound, as in the edematous papillae of active lesions. The blood vessels in the dermal papillae are normal in caliber, although there are many lymphocytes and fibroblasts around them. Chromatophores are frequent in the cutis, particularly beneath areas where no pigment is present in the basal layer.

HEALED NEURODERMATITIC LESIONS

Specimens of healed lesions were obtained from the cubital fossae of 6 patients. Two of these patients had lesions elsewhere, while the other 4 had no noticeable lesions elsewhere at the time of the removal of tissue for biopsy.

Epidermis.—The corneum in healed lesions is as thick as it is in active lesions (table). In recently healed lesions there are not many patches of parakeratotic corneum, but in old healed lesions there is much patchy parakeratosis. Most of the corneum in newly healed lesions is heavily keratinized.

The stratum granulosum is about twice as thick as that in normal skin and of the same thickness as that in active lesions (table). In recently healed lesions the cells of the stratum granulosum contain many granules of keratohyalin, while in old healed lesions the keratohyalin granules seem to have been vacuolated by imbibition of water. Such areas of vacuolated granular cells are found usually under patches of parakeratotic corneum.

The spinous cells in recently healed lesions show a large number of circumnuclear vacuoles that seem to have increased in size as the cells approached the corneum. In old healed lesions, however, none of the spinous cells contains perinuclear vacuoles. The cytoplasm of the spinous cells in healed lesions does not stain well with aniline blue (as in active lesions) but stains with acid fuchsin and appears reddish. In recently healed lesions the intercellular fibrils of the spinous cells are heavily keratinized. Many of the nuclei are pyknotic.

The basal cells of recently healed lesions appear to be normal, except that few of them contain pigment granules. The basal cells and the spinous cells immediately above them are definitely more intensely stained than the distal spinous cells. Even in old healed lesions the basal cells are not heavily pigmented, and their cytoplasm does not stain any more deeply with acid fuchsin than does that in the basal cells of very active lesions. The old healed lesions studied, however, may have been in the preliminary stages of a second attack, which might account for this lack of pigment.

In recently healed lesions the epidermis is acanthotic, being as thick as that in active lesions. In old healed lesions the thickness of the

epidermis is reduced to about half that in active lesions. In recently healed lesions there are many more mitotic figures than in active lesions, and the nonpigmented basal layer contains many more clear cells than it does at any other stage of the disease. The cytoplasm of dividing cells

Fig. 7.—Section from healed neurodermatitic lesion (alcohol-formaldehyde solution; Masson's trichrome stain; × 905), showing clear cell in mitotic division.

is clear and resembles closely that of the clear cells. Occasionally a clear cell of the basal layer may be seen dividing mitotically (fig. 7).

Cutis.—In recently healed lesions thick tightly bound ropelike masses of collagenic fibers cover the apical surfaces of the rete pegs. These fibers do not extend into the dermal papillae. There are many chromato-

phores whose pigment granules leave an iron residue on incineration. The perivascular infiltration has not been reduced in any of our cases (table).

OTHER CUTANEOUS DISEASES

A total of 55 cases of thirteen different cutaneous diseases other than neurodermatitis were studied histologically. Only five of these diseases resemble neurodermatitis closely, namely, lichen simplex chronicus, exfoliative dermatitis, infantile dermatitis, chronic contact dermatitis and psoriasis.

Localized Neurodermatitis.—Localized neurodermatitis, or lichen simplex chronicus, is generally acknowledged to be an essentially different disease from generalized or disseminated neurodermatitis.

From our five specimens, we were unable to distinguish this disease unequivocally as a histologic entity distinct from disseminated neurodermatitis. However, there are certain decided differences that should be recorded. The basal layer of the epidermis almost always consists of a double row of cells that are "piled" on one another in a single row space. These large basal cells have huge nuclei, about twice the size of the basal cell nuclei of disseminated neurodermatitis epidermis, and they are often binucleated. There is not much intercellular edema, for the spinous cells are conspicuously closely packed together, the intervening spaces being filled with rows of deeply stained (ponceau xylidine) intercellular fibrils that are heavily keratinized. In disseminated neurodermatitis the intercellular fibrils are heavily keratinized also, but the spinous and granule cells are widely separated by distended intercellular spaces. In localized neurodermatitis the outlines of the cells are conspicuous by their borders of deeply stained fibrils.

In the skin of every one of our 5 cases there were many large vacuoles embedded in the corneum which were filled with a homogeneous substance stained, in Masson preparations, with a blue collagenophilic dye (aniline blue) instead of with ponceau xylidine, with which the remainder of the keratinized corneum was colored. Such vacuoles were not found in disseminated neurodermatitis skin.

The epidermis of patients with localized neurodermatitis shows many spots where the cells have disintegrated, leaving the overlying epidermis intact. There are many isolated cells in the spinous layer that are not stained at all. These appear to be moribund cells. The epidermis is often invaded by fibroblast-like cells that stain more deeply than the other epidermal cells.

Another striking difference between localized and disseminated neurodermatitis is that the cutis of localized neurodermatitis is thickened by a dense mass of very fine threads of collagenic fibers that are faintly stained with aniline blue, whereas the cutis of disseminated neuroderma-

titis is thickened by a similarly dense mass of coarse collagenic fibers that are heavily stained with aniline blue. In the cutis of localized neurodermatitis there are many blood vessels whose lumens are compressed by the dense collagenic fibers. In disseminated neurodermatitis the comparatively few blood vessels are dilated.

Exfoliative Dermatitis (Idiopathic).—In our 5 cases of exfoliative dermatitis the stratum granulosum was three times thicker (table), although the granules of keratohyalin were much finer, than in our cases of disseminated neurodermatitis. In most places the granules were so fine as to be almost invisible except on examination with an oil immersion lens. The keratohyalin granules of exfoliative dermatitis did not take the hematoxylin in tissue fixed in Zenker's solution prepared with solution of formaldehyde but were colored intensively with ponceau xylidine in identically fixed Masson preparations. Often the granular layer was absent, the spinous cells simply merging into the corneal layer. However, in such areas where the granular layer was missing, the corneum stained only faintly with ponceau xylidine. The intercellular fibrils were heavily keratinized in all cases, as in neurodermatitis. The basal cells in all 5 of our cases of exfoliative dermatitis were more heavily stained with hematoxylin than were the basal cells of neurodermatitis, although in Masson preparations they were faintly stained with acid fuchsin, in contrast to the heavily stained basal cells in Masson preparations of neurodermatitis skin.

Exfoliative dermatitis seems to differ histologically from neurodermatitis in that the corneum and granule cells are keratin poor, whereas in neurodermatitis they are keratin rich. The basal cells of exfoliative dermatitis have a strong affinity for hematoxylin and do not take acid fuchsin stain, whereas the reverse is true in neurodermatitis. This apparently indicates that there is some chemical or physical change in the basal cells that is responsible for a change in the keratinization process.

However, we are not willing to differentiate exfoliative dermatitis as an anatomic entity distinct from neurodermatitis, since the number of our cases is limited.

Infantile Dermatitis.—This cutaneous disturbance is said by some dermatologists to be the forerunner of disseminated neurodermatitis. In the single case studied the condition was certainly, in general, similar histologically to chronic disseminated neurodermatitis. The elongated rete pegs in the case of infantile dermatitis were longer than those of disseminated neurodermatitis, and they were very narrow, even to their apexes (fig. 8), whereas in neurodermatitis they are clubbed and thicker at the apexes (table). The epidermal cells of neurodermatitis are considerably larger than those seen in the case of infantile dermatitis, but in this case the stratum granulosum was much thicker (table)

and there were conspicuously rounded keratohyalin granules. Here, again, as with lichen simplex chronicus, there was no sound histologic basis of distinction between this case of infantile dermatitis and one of neurodermatitis.

Contact Dermatitis (Eczema).—Six of the eight specimens of contact dermatitis were taken from patients suffering from this dermatitis for

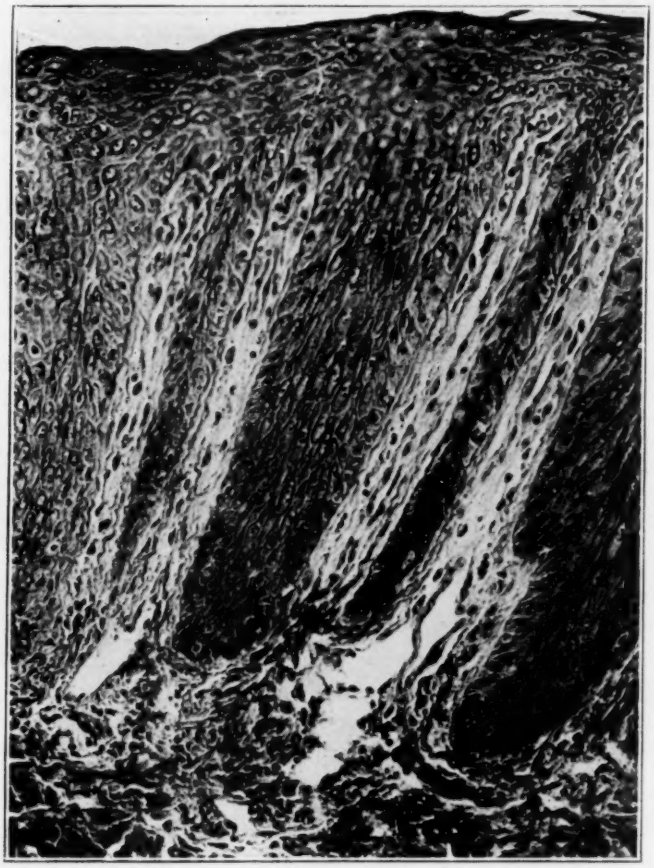

Fig. 8.—Section from active lesion of patient with infantile eczema (alcohol-formaldehyde solution; Masson's trichrome stain; × 195), showing narrow rete pegs.

varying lengths of time; in some the condition was chronic and in others acute. The remaining two specimens were taken from skin under patch tests, and this condition certainly does not illustrate a chronic type of dermatitis.

Chronic dermatitis is more nearly like neurodermatitis than any of the other conditions we have studied. The epidermis, however, is not

generally as thick nor are the rete pegs as elongated as in neurodermatitis (table). Epidermal vesicles were not present in our cases of chronic contact dermatitis, although they may be found in cases of patch test dermatitis. In most cases of chronic contact dermatitis the corneum is not as heavily keratinized (as determined by staining with ponceau xylidine) as in those of neurodermatitis. The basal layer in some cases is pigmented (even hyperpigmented in some areas) in active lesions and almost always in more quiescent stages of the disease.

The rete pegs in chronic contact dermatitis are not close enough together to allow for the formation of expanded (or ballooned) papillae, such as occur in neurodermatitis. The cutis is often invaded by many lymphocytes and eosinophils that surround edematous rete pegs. The endothelial lining of the blood vessels is greatly thickened, but there is comparatively little perivascular infiltration.

In patch test dermatitis and recently developed contact dermatitis only the outer layers of the epidermis are edematous, frequently showing vesicles, and the basal cells contain their usual amount of pigment. The rete pegs are of normal length.

It was difficult to distinguish histologically chronic contact dermatitis in 2 of our cases from chronic disseminated neurodermatitis, except on the basis of difference in the length of the rete pegs and the absence of ballooned papillae. However, recently developed contact dermatitis (patch test dermatitis) is easily distinguishable on the basis of the conspicuous absence of elongated rete pegs and the presence of pigment in the basal cells.

Psoriasis.—To state that in every one of our 13 cases of psoriasis the condition was histologically distinguishable from chronic disseminated neurodermatitis seems somewhat unorthodox. This, however, was the case, and we feel reasonably certain that the differences were not artifactitious, since the histologic tissue was fixed by three different methods (dehydrated alcohol and solution of formaldehyde, Zenker's solution prepared with solution of formaldehyde and Bouin's fluid) and were sectioned and stained by two different investigators in two different ways from the same biopsy specimen. The lesions of psoriasis varied considerably in their structure, but all of them could be readily distinguished from those of chronic disseminated neurodermatitis. Of course, microabscesses of Munro could be found in almost all of our cases, but even in areas where such abscesses and migratory lymphocytes were absent, psoriatic lesions were easily distinguishable from those of neurodermatitis.

In the first place, in every case of psoriasis there were intraepidermal patches of tortuous dermal papillae (fig. 9), which were the result of acanthosis and not of oblique sectioning, for each biopsy specimen was cut at two different angles. These intraepidermal patches of dermal

papillae were numerous and were an unmistakable characteristic in every one of our cases except 1, which was a case of surface involvement without epidermal changes and in which there were only a few intraepidermal dermal papillae.

Fig. 9.—Section from active lesion of patient with psoriasis (alcohol-formaldehyde solution; Masson's trichrome stain; × 345), showing intraepidermal patches of dermal connective tissue.

Another pronounced histologic characteristic of these psoriasis specimens was the breadth of the acanthotic rete pegs, which were often five times wider at the apex than were the narrow neurodermatitis rete pegs (table and fig. 10). It appeared as though several rete pegs

had fused at their apexes. In only one specimen of the 13 cases of psoriasis did we find a single place where the rete pegs at all resembled those of neurodermatitis. Only two of the pegs in this whole section were indistinguishable from those of neurodermatitis.

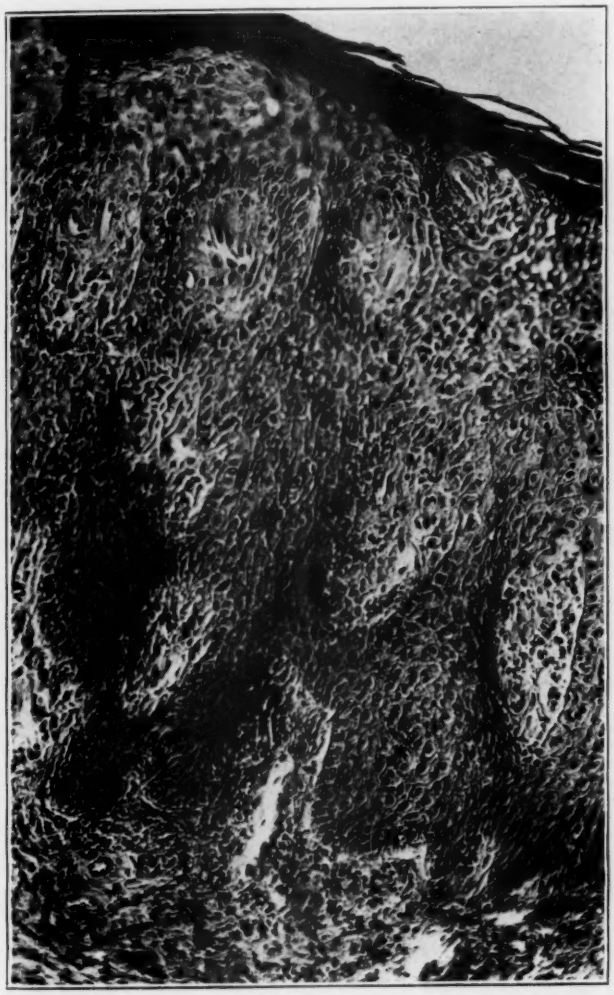

Fig. 10.—Section from active lesion of patient with psoriasis (alcohol-formaldehyde solution; Masson's trichrome stain; × 160), showing broad coalesced rete pegs and intraepidermal cutis.

The microabscesses of Munro were not nearly so characteristic in our cases as they seemed to be in cases described by other investigators. There was in every case, however, a considerable number of migratory leukocytes in the epidermis in some areas. There were frequent patches

of extravasated blood that had formed small vesicles between the corneum and the stratum granulosum.

The blood vessels assumed a much greater diameter in psoriasis; the endothelial lining cells were vastly larger than those of neurodermatitis (table), and the dermal infiltration consisted chiefly of white blood cells whose nuclei were larger and stained less intensely than those in neurodermatitis infiltrates.

Although we realize that many cases of aberrant psoriasis which closely resembled neurodermatitis histologically have been described,[16] we must nevertheless point out—for the sake of clarity in the description of our incinerated sections (to be published)—that our cases of psoriasis were histologically distinct from our cases of chronic disseminated neurodermatitis, even though these diseases may not be distinct from other diseases.

COMMENT

The Development of a Lesion.—During the course of this investigation of neurodermatitis particular stress was laid on the histologic differences between various stages in the development of a lesion. Specimens of unaffected skin, of mildly active lesions, of active lesions, of recently healed lesions and of old lesions were obtained whenever possible. In view of the limited number of such cases, it is with some degree of caution that we present the account of our conception of the processes involved in a developing lesion as a basis for the description of the mineral studies to be described in subsequent papers.

At the outset of neurodermatitis the skin at the site of the future lesion in the affected area is undoubtedly similar to the unaffected skin elsewhere on the body, where lesions never appear. The same sort of processes as occur in areas of active lesions also occur in the unaffected skin in the region of the midaxillary line, but to a less conspicuous degree.

The preliminary site of the developing lesion is highly pigmented in most places and hyperkeratotic in nonpigmented areas. The nonpigmented areas are probably the most vulnerable ones. There is an unusual amount of perivascular infiltration, although the caliber of the blood vessels is normal. The epidermis is slightly acanthotic, especially in nonpigmented areas. The intercellular fibrils and the nucleoli are heavily keratinized in areas of hyperkeratosis. The spinous cells are larger than normal spinous cells.

The first reaction is probably a change in the chemical constituents of the spinous cells, which results in the keratinization of the intercellular fibrils and of the nucleoli. Such a change might be con-

16. MacKee, G. M., and Foster, P. D.: Histopathogenesis of Psoriasis and Its Aberrant Lesions, Arch. Dermat. & Syph. **34**:35 (July) 1936.

ceivably traced to the blood vascular system, since there is considerable perivascular infiltration. The perivascular infiltrate is most conspicuous in nonpigmented areas. Perhaps excess amounts of glutathione were supplied to the epidermis, and the basal cells became unable to bind it into melanin. Its components may therefore have damaged the spinous cells immediately above them, causing not only hyperkeratinization but also imbalances in mineral constituents. It is difficult to localize the primary shock tissue in neurodermatitis, since so many deviations from the normal structure appear in the same tissue. Any explanation of them must for the present remain hypothetic, because a complete chronologic story is lacking.

The earliest lesion we were able to obtain was completely depigmented. Such a loss of pigment must have been exceedingly rapid. Nowhere was pigment to be found except in a few chromatophores of the cutis that contained iron, which was probably ingested from blood extravasations. The rete pegs were slightly elongated, and there was little evidence of edema. Obviously, the most complete detectable reaction that takes place at first is the process of depigmentation.

In the later active lesion, the epidermis is much more thickened; the rete pegs are elongated, and the dermal papillae are distended by edema. The hyperkeratinization has reached its peak of activity, and most of the blood vessels are dilated with some parts of their walls embedded in clumps of lymphocytic infiltrates. These clumps of infiltrated white blood cells are limited to the vessels near the apexes of the rete pegs and are absent in the dermal papillae.

The second stage of the developing lesion consists largely of a thickening of the epidermis by acanthotic processes and by hypertrophy of individual cells, and of a decided deposition of keratin, formed as a result of the dissolution of an excess amount of pigment.

The last process that occurs is the thinning and ultimate breakdown of the epidermis overlying the edematous papillae. After this there is a mobilization of certain clear cells which probably act as phagocytes, melanoblasts and, particularly, regenerative cells to supply a new epidermis. Hyperpigmented patches develop, and much of the corneum becomes parakeratotic and hyperkeratotic alternately. This temporary and fluctuating condition then persists probably until the next attack.

The Nature of Clear Cells.—Masson [17] suggested that the clear cells invading the basal layer of the epidermis are the precursors of dendritic or pigment-forming cells. We are not entirely satisfied that this hypothesis explains some of our observations in specimens of neurodermatitis skin. In neurodermatitis and in normal skin the clear cells do not seem

17. Masson, P.: Les naevi pigmentaires, tumeurs nerveuses, Ann. d'anat. path. 3:417, 1926.

to be related to melanogenesis, for they appear in larger numbers in nonpigmented than in pigmented epidermis, and in many nonpigmented areas there are no clear cells present. In an active lesion of neurodermatitis, for example, there may be many clear cells invading the areas of a disintegrating nonpigmented epidermis, while in other nonpigmented areas of the same epidermis there are no clear cells anywhere. It may be supposed that a certain time factor may account for the presence of many clear cells in nonpigmented epidermis, since the appearance of dopa-positive dendritic cells may precede the actual formation of pigment [18] by a considerable period of time, during which the dendritic cells may disappear before the visible pigment granules are formed. If a time factor is assumed, it is difficult to explain the fact that melanomatous growths are studded with numberless clear cells in both hyperpigmented and nonpigmented, dopa-positive melanomas. However, the dopa-oxydase theory of melanogenesis is still unproved, for it is difficult to explain the fact that the dopa reaction and also postmortem pigmentation can be obtained in sections of boiled skin.[19] Furthermore, clear cells are frequently found in the prickle cell layer, while dopa-positive dendritic cells are confined to the basal layer.

On the other hand, in our cases of xeroderma pigmentosum there were many clear cells in the heavily pigmented areas and the basal cells were loaded with melanin. In nonpigmented spots clear cells may or may not be present. The nonpigmented epidermis of xerodermatous skin, which possesses many large clear cells, is always hyperplastic, showing numerous mitotic figures and sometimes binucleated clear cells in the basal layer, although the prickle cell layer is atrophied. In pemphigus epidermis which is nonpigmented great numbers of clear cells invade the basal cell layer. Even in the comparatively few hyperpigmented spots of pemphigus skin the clear cells are numerous. In our cases of these diseases there seemed to be no consistent order of the presence or absence of clear cells in relation to the degree of pigmentation of the epidermis, and our observations did not lend much support to Masson's theory of the melanogenic function of these cells.

Clear cells in normal skin, however, do not closely resemble those found in our pathologic skins. The clear cell in normal epidermis is smaller, with a usually crescentic densely stained nucleus (which resembles that of a moribund cell) and with cytoplasmic strands stretched around clear spaces to a thin peripheral cell wall. The clear cell in neurodermatitis skin generally possesses a homogeneous cytoplasm with-

18. Peck, S. M.: Pigment (Melanin) Studies of the Human Skin After Application of Thorium X, Arch. Dermat. & Syph. **21**:916 (June) 1930.

19. Heudorfer, K.: Untersuchungen über die Entstehung des Oberhautpigments und dessen Beziehung zur Addisonschen Krankheit, Arch. f. Dermat. u. Syph. **134**:339, 1921.

out large vacuoles and a large, round, faintly stained nucleus. These clear cells of neurodermatitis and other diseases are at least twice as large as normal clear cells. It is entirely possible that there are several kinds of clear cells. Masson [20] went so far as to suggest that certain clear cells in human epidermis, which he thought were precursors of melanomatous growths, were derived from the cells of the sheath of Schwann.

It seems that in neurodermatitis the clear cells are more frequently related to regeneration of new epidermis than to any other physiologic phenomenon, for in recently healed lesions that show large numbers of faintly stained mitotically dividing basal and spinous cells, the clear cells invading the basal layer are unusually numerous. Occasionally clear cells may be seen dividing in the basal layer. Many clear cells are found in any area of neurodermatitis skin where active mitosis and thickening of the epidermis is occurring. This relation to regeneration is far more consistently uniform than is the relation of clear cells to pigmentation.

The Relation of Pigmentation to Keratinization.—The process of pigmentation seems to be definitely related to keratinization in neurodermatitis. During the development of a lesion in this disease, the basal cells that were once heavily pigmented lose their melanin, and at the same time there is an increase in the number and size of the keratohyalin granules and the corneum becomes heavily keratinized and thickened. While the depigmentation is progressing, there is also a decided hyperkeratinization of the intercellular fibrils (i. e., they stain heavily with ponceau xylidine). In areas of heavily pigmented basal cells the intercellular fibrils are not usually heavily stained with ponceau xylidine. Areas of unaffected neurodermatitis skin that are heavily pigmented do not show hyperkeratosis or thickening of the intercellular fibrils. The corneum of all depigmented areas of skin is decidedly hyperkeratotic, while all heavily pigmented areas are normally keratinized or parakeratotic. This suggests that as long as the excess pigment in the basal cells remains intact, the manufacture of keratin proceeds either at normal speed or is slowed to a point at which parakeratosis with keratin-poor cells occurs.

Another interesting histologic change in neurodermatitis skin is in the staining capacity of the nucleoli of basal and spinous cells. Normally only one of the nucleoli stains heavily, while the others stain faintly with acid fuchsin. In active lesions of neurodermatitis skin these nucleoli all stain intensely, not with acid fuchsin but with ponceau xylidine, indicating a similarity of their constituents to keratin or

20. Masson, P.: Les cellules de Langerhans: Leur rôle dans les échanges dermatoépidermiques, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **28**:7, 1921.

keratohyalin. Ludford [21] stated the belief that the nucleoli are active participants in the formation of keratohyalin granules. While we have not observed any clearcut evidence of the extrusion into the cytoplasm of nucleolar substance, as Ludford described, it is not unlikely that such a process may occur. This change in the staining capacity of nucleolar elements is most evident in areas where the basal cells have lost their melanin. It may be the result of the sudden release of some component of pigment at the time of melanolysis.

It is well known that both melanin and keratin are rich in sulfur. Glutathione, which seems to accumulate as the epidermis is formed and as melanogenesis is progressing, disappears as keratin is formed.[22] Perhaps the rapid formation of keratin in the hyperkeratosis of depigmented neurodermatitic lesions merely represents the binding of free sulfur that is released by the splitting of glutathione which is not normally bound into melanin. Morse [23] suggested that gluthathione is the precursor of a molecule of glutamic acid, cystine and aminoacetic acid in keratin. Ropshaw [24] stated that melanogenesis results from the reaction of cystine on protamine and is therefore limited in the skin to the epithelial layer, the only one containing sulfhydrils. He also stated that the reaction occurs only in the presence of protamines that contain iron. Cowdry [25] suggested that the gradual decrease in oxygen supply to peripheral epidermal cells may be a factor in the mechanism of kenatinization.

In our cases of xeroderma pigmentosum, the basal cells of the epidermis were usually heavily pigmented, and at the same time the corneum was hyperkeratotic. This at first seems contradictory. But if one observes such cases closely, it will be seen that although there is a great deal of pigment being formed in the basal cells, it is passed off to the peripheral layers of the epidermis, for many of the spinous cells contain some pigment. As the spinous cells move toward the stratum granulosum, they gradually lose their melanin, so that melanolysis occurs in passage. Furthermore, the greatest hyperkeratosis in this disease is seen over areas of completely depigmented basal cells.

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21. Ludford, R. J.: Cell Organs During Keratinization in Normal and Malignant Growth, Quart. J. Micr. Sc. **69**:27, 1924.

22. Giroud, A., and Bulliard, H.: Glutathion de kératine, Compt. rend. Soc. de biol. **98**:500, 1928.

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25. Cowdry, E. V.: Special Cytology: The Form and Functions of the Cell in Health and Disease, New York, Paul B. Hoeber, Inc., 1932, vol. 1.

SUMMARY

The histologic structure of the skin in 33 cases of chronic disseminated neurodermatitis is described and compared with that of the skin of similarly aged normal persons and that of the skin of patients with other cutaneous diseases.

Unaffected skin from patients with neurodermatitis is found to be hyperpigmented and hyperkeratotic, with a slightly acanthotic epidermis.

Skin from active lesions is hyperkeratotic, acanthotic and completely depigmented. Perivascular infiltrations are common in the subpapillary cutis. The nucleoli and intercellular fibrils of the spinous cells are heavily keratinized.

In healing lesions, in which there are many mitotically dividing cells, the basal layer is found to be thickly beset with many clear cells.

Although chronic disseminated neurodermatitis is not found to be an anatomic entity, examples of this disease were easily distinguishable from 13 examples of psoriasis and from 8 of contact dermatitis.

The clear cells in the basal layer of the epidermis appear to be concerned in regeneration rather than in pigmentation.

Evidence is presented to show that pigmentation is definitely related to keratinization.

The development of a typical neurodermatitic lesion is described. The first detectable reaction is a change in the spinous cells during depigmentation of the basal layer.

SKIN REACTIONS

XII. PATTERNS PRODUCED IN THE SKIN BY ELECTROPHORESIS OF DYES

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It is customary to consider that the glands of the hair follicles furnish the most important living membrane through which materials may pass through the skin.[1] However, the fact that the comparatively large molecules of ragweed and timothy extract may be readily transported by electrophoresis into the human skin [2] led to a reexamination of the channels which take part in the transport of materials in the human skin.[3] It was pointed out that in reality three main channels must be considered: (1) the pores, or coils, of the sweat glands; (2) the hair follicles and the sebaceous glands, and (3) the skin itself, that is, the keratin matrix linking the structures mentioned in (1) and (2). It was shown that by means of electrophoresis of positively charged dyes like methylene blue (methylthionine chloride) and of negatively charged dyes like azosulfamide (disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonate), and phenolsulfonphthalein, it was possible to develop a pattern merely by rubbing off the dye staining the superficial layers of the skin. The details of the method of producing pore patterns and the theory have been published.[4] The present communication serves the purpose of making the method known to dermatologists by illustrating typical patterns in cutaneous conditions of special interest to dermatologists.

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From the Department of Physiology, Columbia University College of Physicians and Surgeons, and the Medical Service of Dr. George Baehr and the Laboratories of the Mount Sinai Hospital.

1. Fantus, B.: General Technic of Medication, ed. 3, Chicago, American Medical Association, 1938, p. 28.

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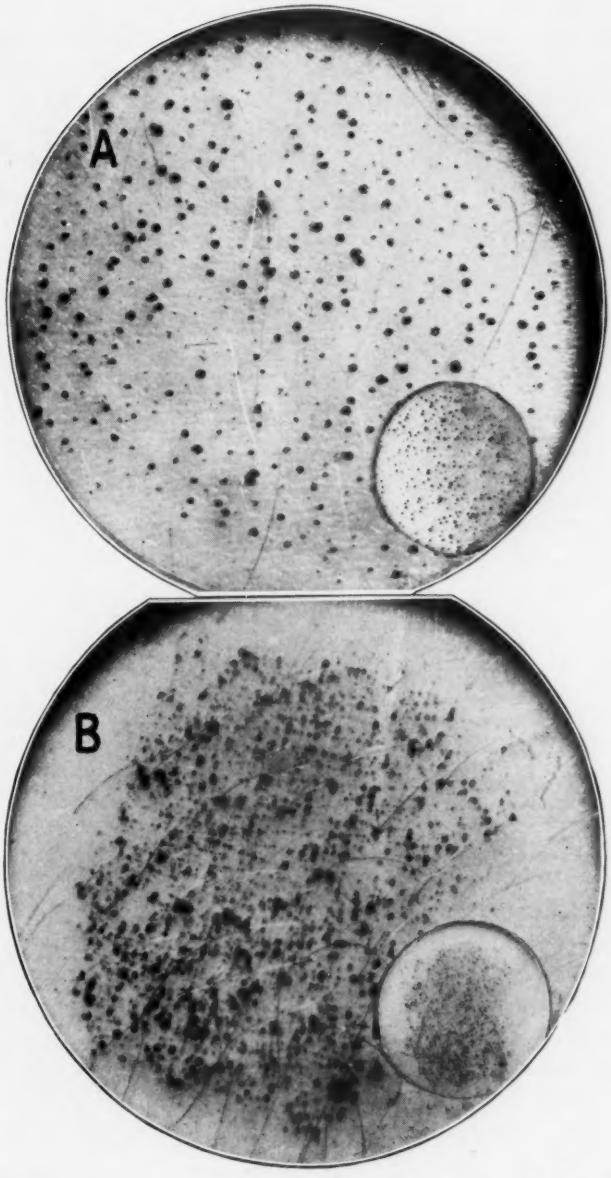

Fig. 1.—Pore patterns (× 3.2; inserts, natural size: *A*, on the anterior aspect of the forearm of a man. *B*, on the arm of a normal woman. In the lower central portion is a large doughnut form, probably a stained sebaceous gland orifice.

NORMAL CONDITIONS

Patterns Obtained by Electrophoresis of Methylene Blue.—In the skin of the forearm: In figure 1 are types of patterns obtained by the electrophoresis of methylene blue (methylthionine chloride) in the arm. It must be noted that this type of pattern is obtained only after the excess dye has been removed by vigorous rubbing. The pore pattern in the forearm of a male is different from that in the upper part of

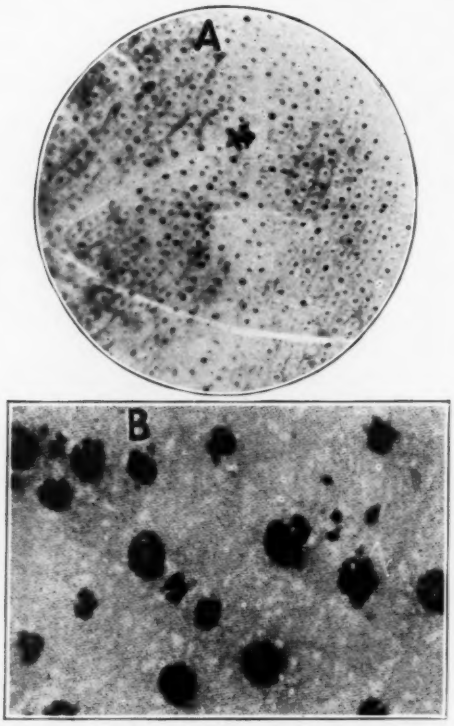

Fig. 2.—Pore patterns: *A*, in the palm of a man, illustrating the sweat glands. *B*, the doughnut form, due to deposit of dye in the sweat glands on the anterior aspect of the forearm (× 12).

the arm of a female, although differences of this type are not always observed.

In the skin of the palm: Another example of pore patterns was obtained in the normal palm of an adult male, the result of electrophoresis of 2 per cent methylene blue in 50 per cent glycerin for ten minutes (fig. 2 *A*). Close examination of the patterns illustrated indicates that the dye is not transported into the hair follicles but that it is deposited in the orifices of the sweat glands and then apparently in the orificial cells of the sweat glands themselves (although histologic studies of this

point have not been made). There is other evidence which indicates that living cells are engaged in the staining process. This is observed when certain oxidation-reduction indicators which are rapidly reduced are employed. Indeed, the variations in response to different oxidation-reduction indicators may provide a useful method of studying physicochemical properties of many dermatologic conditions. Studies of this type have been begun in our laboratories.

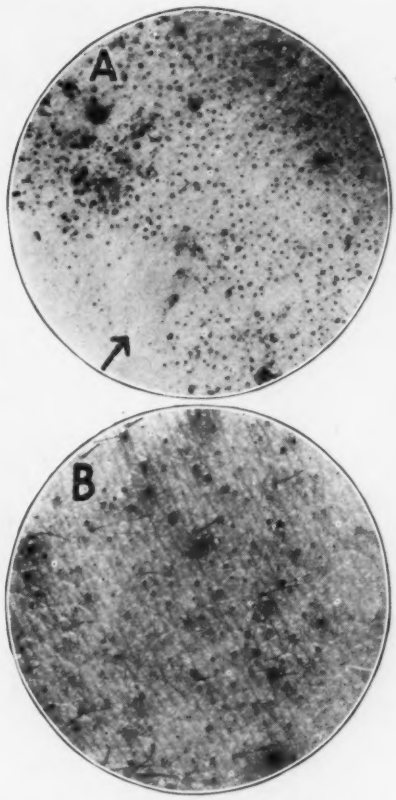

Fig. 3.—Pore patterns (× 3.2): *A*, on the forehead of a woman. The arrow indicates a small scar with no visible pores. *B*, more diffuse staining following the electrophoresis of azosulfamide.

Doughnut Forms: Pore patterns produced with methylene blue may remain clearly visible for as long as two or three weeks. In the course of time, depending on the nature of the dye and the technic, an important transformation may occur in the appearance of individual spots of blue which comprise the pattern. This transformation is well shown in figure 2 *B* and will be subsequently observed in other figures, although not as clearly. Note that the blue spots which have within them paler

white areas have the appearance of doughnuts. Examination of the size and structure of these doughnut forms indicate that the methylene blue which persists is in all likelihood due to a selective staining of the orificial cells of the walls of the sweat glands. The pale areas com-

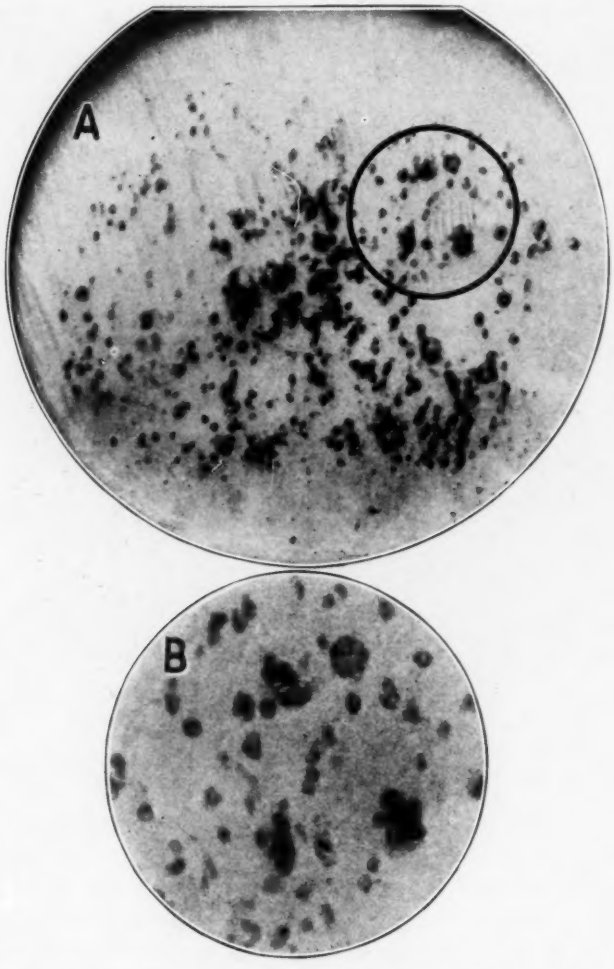

Fig. 4.—*A*, pore pattern obtained with the electrophoresis of methylene blue through a vaccination scar thirty years old. Distorted doughnut forms are readily observed, indicating that in all likelihood physiologically active pores are still present in the scar. *B*, higher magnification (× 8) of the encircled area in *A*.

prising the centers of the doughnut forms are probably the orifices of the sweat glands with the dyestuff itself contained within the cells. Similar pore patterns have been obtained on various parts of the body. The skin of the face, back, chest, abdomen, thigh, legs and dorsa of the

hand, fingers and feet has been investigated. For example, figure 3 *A* shows a pore pattern obtained on the forehead of a normal adult female. Note the larger glands which are, in all likelihood, the sebaceous glands of the forehead. Evidently sebaceous glands of this type also take up methylene blue. Not only do differences exist in different parts of the skin of the same person but the response to the electrophoretic technic in different persons is apparently different as in figure 1. These aspects have not been studied in detail.

Patterns Obtained by Electrophoresis of Other Dyes.—Not only positively charged dyes are transported by electrophoresis but dyes which

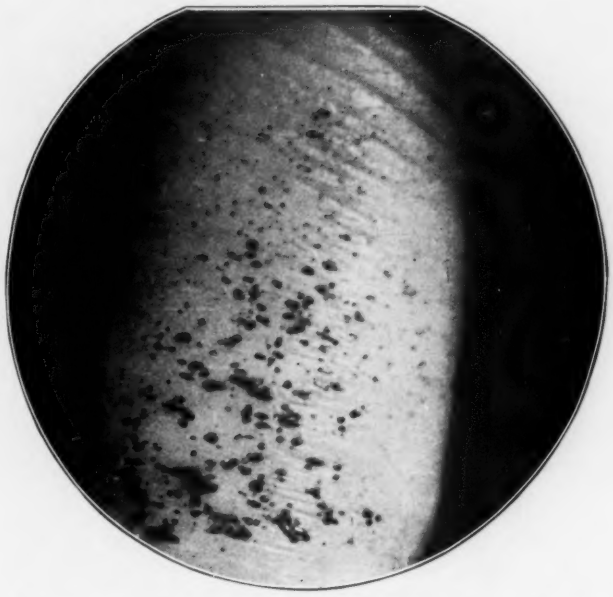

Fig. 5.—A pore pattern in a patient with diffuse scleroderma (× 3.2).

are negatively charged may also be effectively introduced in this way in spite of the negative charge of the skin. This relation between the charge of the dye and the charge of the skin has been a subject of controversy.[4] Figure 3 *B* illustrates well that azosulfamide (disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonate) may be introduced into the skin by the negative pole. Prontosil itself may also be employed. The dye which stains more diffusely disappears more rapidly. Whether this disappearance is due to diffusion or to reduction has not been ascertained. Doughnut forms are also readily observed with negatively charged dyes like prontosil and sodium indigotetrasulfonate. With the latter dye, doughnut forms may appear within two hours. The persistence of doughnut forms for long

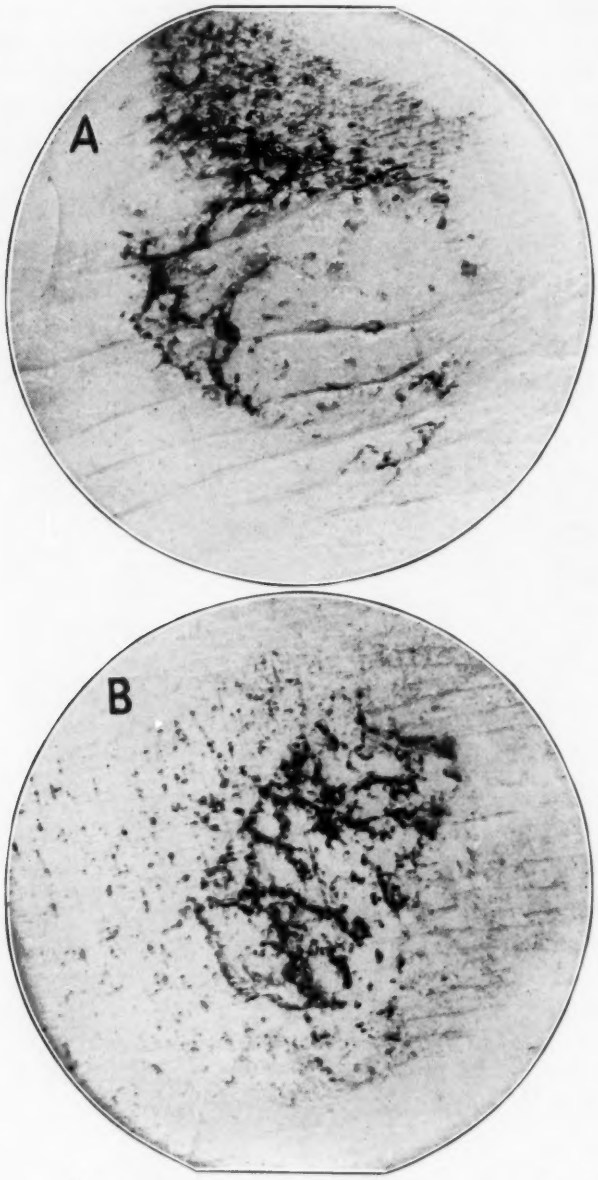

Fig. 6.—Pore patterns (× 3.2): *A*, pattern obtained with methylene blue from a patient with psoriasis. *B*, pattern obtained in a later stage of the disease.

periods with both negatively and positively charged dyes indicates that some kind of chemical binding exists between the substances in the cells comprising the orifices of the sweat glands and the dyestuff. An analogous mechanism may be involved in the maintenance of histamine depots in the skin.

PATHOLOGIC CONDITIONS

Scars.—Surprisingly good examples of pore patterns were obtained by introducing methylene blue by electrophoresis into scars. Scars with

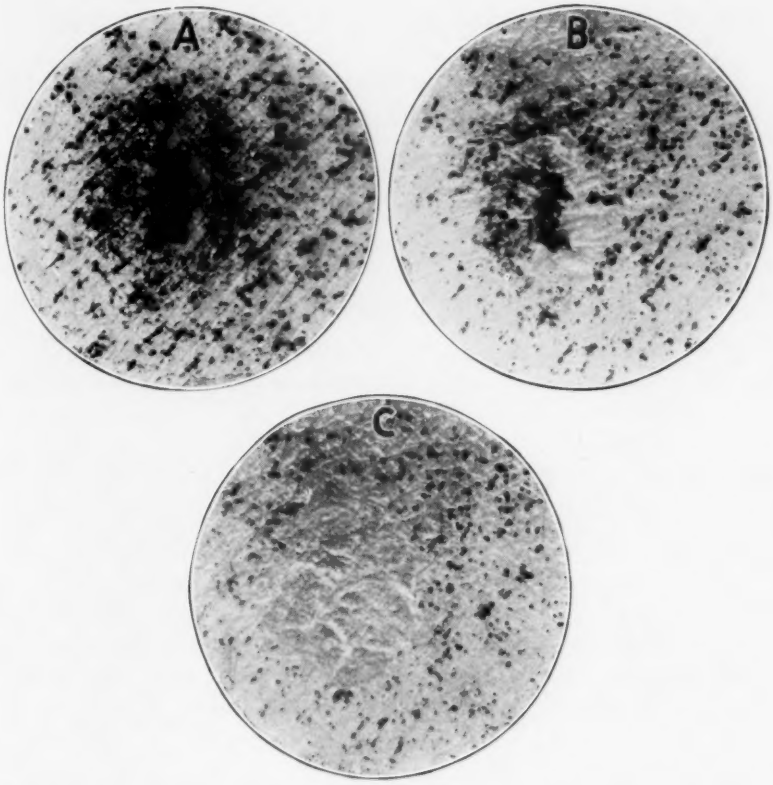

Fig. 7.—*A*, pore pattern (× 3) obtained in patient with pityriasis rosea with methylene blue. *B*, two days later. *C*, exfoliation of the densely stained material (7 *A*) has occurred after five days. There are, however, pores still stained surrounding the main lesion.

an area larger than the applied electrode must be employed for scientific studies of this kind so that the current distribution is fairly uniform within the area of the scar itself. In figure 4 large numbers of electrophoretically patent pores are shown in the scar, which correspond to the sweat glands (fig. 4 *B*). These pores are not circular, and the distortion

is probably due to skin stresses set up by scar formation. Similar pore patterns have been obtained in a scar due to a burn, thirty years old.

Scleroderma.—Figure 5 illustrates a pore pattern obtained on a finger in a case of diffuse scleroderma and shows distorted doughnut forms locating the presence of pores.

Psoriasis.—An insufficient number of cases of this disease have been studied to justify the point of view that patterns such as those in figure 6 characterize the disease.

Pityriasis Rosea.—The changes in the skin incidental to the exfoliation of the tissues containing the methylene blue are illustrated in figures 7 and 8.

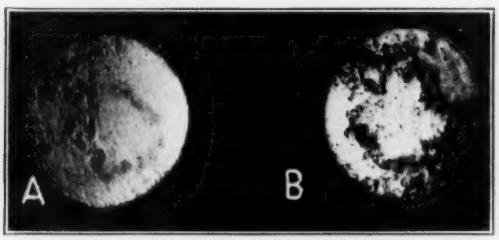

Fig. 8.—Pore pattern (natural size) obtained during late stage of pityriasis rosea: (*A*) unstained and (*B*) after electrophoresis of methylthionine chloride.

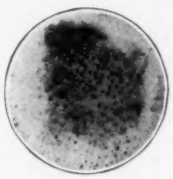

Fig. 9.—Pore pattern (natural size) in the skin of the anterior aspect of the forearm precipitated by electrophoretic epidermal tattooing with silver sulfide.

COMMENT

The electrophoresis of dyes is not the only means by which pore patterns of the type illustrated may be obtained. It has previously been pointed [4] out that copper may be forced by electrophoresis into the pores in a similar way, and it has now been found that the electrophoresis of the silver ion may be readily traced in a similar fashion (fig. 9). The details of this manner of epidermal tattooing by silver sulfide as well as applications to dermatologic conditions will be described in a future communication.

The quantity of electricity transported across the various parts of the skin determines to a certain extent the nature of the pattern. In any event, one may speak of electrophoretically patent pores as being obtained

by the method described. There are, of course, other pores in the skin. These may be brought out by other methods; but certainly as far as water-soluble substances are concerned, electrical transport takes place primarily through the sweat glands and certain of the sebaceous glands rather than only by the hair follicles or the interfaces of the keratinaceous matrix. This has also been demonstrated in unpublished data obtained with silver sulfide patterns.

It is too early to state that the electrophoretic technic may provide dermatologists with diagnostic patterns. But it would certainly seem jusified to state that the ease with which dyes and metals may be localized in the skin following electrophoretic treatment of areas of skin by this technic makes it appear likely that improvements in the electrophoretic mapping and therapy of cutaneous diseases may be anticipated.

The sweat glands have apparently not been considered to be of much significance in absorption from the skin. Fantus [1] in 1938 stated:

> In normal skin, the only layer of living cells through which substances may be absorbed with any degree of ease is the lining of the sebaceous glands. As these are filled with fat, lipophile, i. e., fatty, fat-soluble or fat-solvent substances can penetrate into or through them; hydrophile bodies only when presented in a fatty medium.

This statement, on the basis of our experiments, requires a certain amount of revision. It appears likely that the ducts of the sweat glands and the cells of the sweat glands themselves may also provide a means by which water-soluble materials may penetrate the living human skin. Especially is this so if the penetration is aided by the galvanic current. Ordinarily, the direct electric field merely accentuates diffusion processes which take place spontaneously because of the kinetic energy of the molecules involved. One may therefore, under certain conditions, work back from data obtained by electrophoresis to interpret what might occur by diffusion alone, if specific electrical effects are neglected. A fairly common and interesting type of cutaneous absorption observed in persons who are allergic is the skin reactivity to pollen or food extracts by direct contact. Thus, it is not unusual to find that the skin shows whealing without injection and without electrophoretic administration after contact with timothy extract, ragweed extract or the white of egg. We have recently observed decided whealing to timothy extract by splashing of a glycerinated extract on the thigh. There was no evidence that this was due to indiscernible lesions in the skin. Fantus [5] also stated: "Glycerin has a tendency to retard absorption." This statement should be modified to read: "Glycerin has a tendency to retard absorption in certain cases, but the retardation of water-soluble materials which are not fat soluble may not be important."

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5. Fantus,[1] p. 30.

The data on pore patterns also furnish evidence regarding the mechanism of the reaction to the patch test. The response to patch tests with metallic salts, like nickel, or antigens may depend on the fact that the sweat ducts of the skin are filled with liquid which forms bridges between the cells of the sweat glands and the material on the patch. These liquid bridges serve as channels through which diffusion may occur. There is no evidence, to our knowledge, that when patch tests with water-soluble materials are made the sweat glands may not play an important role.

SUMMARY

A method of mapping the electrophoretically patent pores of the living human skin in health and in disease by means of the electrophoresis of dyes is described. Specifically, pore patterns of scars, scleroderma, psoriasis and pityriasis rosea are illustrated. The relation of the electrical transport of water-soluble materials to the transfer of water-soluble substances by absorption through the sweat glands is discussed.

ORDINARY BALDNESS

PRESIDENT'S ADDRESS

HERBERT RATTNER, M.D.

CHICAGO

> Time himself is bald and therefore to the World's end
> will have bald followers.—*Shakespeare.*

I have chosen to discuss the subject of ordinary baldness, not, as one might think, because of my slight personal experience with it, but rather for its story, which is an old and fascinating one. At one time baldness was considered a mark of indignity—evidence of the wrath of the gods for some sinful indiscretion, a curse, a tragedy. Now, for the many, it is simply one of life's inevitable misfortunes. The subject of baldness has always had comment appeal, some of it in ridicule, some in defense. Baldness, it is said, lends dignity; it becomes one whose responsibilities are weighty; it is the outward sign of an intensely active mind; it attacks thinkers rather than doers. All this is admitted, yet "Ugly is a field without grass, a plant without leaves or a head without hair." And because man has never been obtuse to vanity, he has searched frantically down through the ages for ways to avoid baldness and to overcome it. The search today is no less zealous and, unfortunately, no less fruitless.

Apparently the human hair, as well as the lack of it, has always intrigued man. It is recorded that the Voguls believed that the hair concealed a soul and that to cut the hair from a man was to separate him from his soul. The origin of scalping was thought to be based on this belief, the savage scalping his enemy to prevent his ghost from walking. The hair's particular function has usually been of no importance other than to serve as an ornamental frame for the face, yet there have been times when hair had special significance in religious, political and even social position. The freeman, for instance, was distinguished from the slave by the length of his hair; the Cavalier was known by his curls and the Puritan by his "polled" head. At one time the hair was supposed to be a measure of the character of a person, of his temperament, of his powers and of his habits of thought. Black hair, it was thought, indicated athletic strength, vigor, energy, ambition and the passions—a direct contradiction to Sabouraud's dictum that it is the

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bald-headed men who are "mâles très mâles." Conversely, fair hair is supposed to represent a soft and lax fiber and is the emblem of mildness, tenderness and affection, blended with judgment, in short, all the qualities which are usually associated with a calm, sweet temperament. It would seem from this, then, that gentlemen prefer blonds not without some reason.

The legend of Samson long has been cited to prove that strength lies in the luxuriance, vigorous growth and proper functioning of the hair and that to be suddenly deprived of hair is to cause physical weakness, to enervate the frame and to weaken the understanding. There was much ado on this score when Rodama, an African king, in the interest of cleanliness, first introduced the cutting of hair to his soldiers. They complained of headache and dizziness and "their women set no bounds to their clamor (for other reasons), for it had been their pride to dress their husbands' hair and to vie with one another in the creation of elaborate hairdresses." [1]

In Biblical times the practice of shaving the head in token of great sorrow and humiliation for sin was common among Jews. Thus Isaiah stated: "In that day did the Lord God of Hosts call to weeping, mourning and to baldness." The Egyptians, too, expressed grief by cutting the hair, with the idea evidently that mourners should divest themselves of that which man deemed most ornamental, an idea that has been the basis of mourning in all ages. The ancient Syrians were forbidden to make themselves bald in the manner of the heathen, Bacchus, except as an offering to the gods.

A lack of hair from natural causes, on the other hand, was deemed a curse, and in the Scriptures it is recorded that the prophets actually applied it as a denunciation of judgments. Ezekiel proclaimed, "And shame shall be on all faces and baldness upon their heads." "Go up, thou baldhead!" was a favorite term of reproach and contempt among the ancients. Today the same contempt is in the expression, "Get going, curly!"

Apparently bald heads became too numerous to hold them all up to scorn, and, too, some of them must have rested on important shoulders, for soon baldness became an indication of great intelligence, wisdom, eloquence and even affluence. Affluence, indeed: Thus contempt gave way to ridicule and ridicule to tolerance, and finally these compensating mechanisms seemed to make of baldness an actual virtue. A vague notion was formulated that abundance of hair denoted a lack of brains, and from this idea arose the proverb, "Bush natural, more hair than wit." Man, according to this thesis, became bald from the greater excitement of the brain which intellectual pursuits occasioned. The

1. Rowland, A.: The Human Hair, London, Piper Brothers & Company, 1853.

scientific explanation for this was that an irritable condition of the brain due to cerebral congestion reflexly interfered with hair growth, because the nerves supplying the scalp are directly connected with those supplying the pia mater and the dura. Baldness was noted less often among those engaged in manual labor and more frequently among men of science and literature, ministers, lawyers and even legislators. It was not so long ago that Eaton stated, as proof of the greater prevalence of baldness among the intellectual and educated classes, that in church and at the opera 40 to 50 per cent of the men were bald, whereas in the audiences of cheap museums and prize fights the average incidence was less than half this percentage.[2] I should be the last one to question this interpretation, but the thought does occur: Where else but to church or to the opera can a bald-headed man go with complete comfort? The familiar picture of a bald-headed barber rubbing tonic into the scalp of a man with thinning hair might conceivably be an indication of wisdom and eloquence, but only on the part of the barber. The anxious patient who repeatedly consults the bald-headed dermatologist is additional evidence which weighs heavily against the belief that it is the bald-headed who are the intelligent. Alopecia, the generic name for baldness of any type, is derived from the Greek word meaning fox, because the fox is much subject to patches of baldness. The cunning of the fox is well known. Can it be that the prestige for wisdom which attaches itself to baldness in man is also derived from the fox? If a myth, in its relation to medicine, is something existing only in the imagination, the intelligence theory of baldness is certainly only a myth. Yet the claim for a link between intelligence and baldness, old as it is, lives even today. In the newest authoritative textbook of dermatology, the authors, both of whom have hair, but little to spare, modestly state that baldness is "undoubtedly more common in the brainy types." [3]

REMEDIES

But despite a host of similar nugacities—"The bald-headed man will be master of his own house"; "Thick hair, thick head"; "What He hath scanted man in hair, He has given him in wit," and "Grass will not grow on busy streets"—aimed to console the bald, through the ages there has been a frenzied search both for remedies against baldness and for its causes. The ancients used magic pomades; the moderns still employ pomades, and with equal success. A favorite Egyptian remedy for baldness consisted of equal parts of the fats of the lion, hippopotamus,

2. Stelwagon, H. W.: Treatise on Diseases of the Skin, ed. 6, Philadelphia, W. B. Saunders Company, 1910, p. 955.

3. Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, Philadelphia, J. B. Lippincott Company, 1940.

crocodile and serpent. Others used bear grease, for the grease of fur-bearing animals has always held favor. "Ashes of little frogs, burnt, applyd suddenly, cureth the Fall of Hair." [4] Burnt ashes of goats' dung anointed with oil was used to multiply the hair, as was dogs' urine when applied to the head. Less than one hundred years ago it was recommended that garden snails be plucked out of their houses and pounded with horse leeches, bees, wasps and salt, an equal quantity of each, and that after the mixture had been buried eight days in a hot bed, it be applied to the area of baldness. Also recommended were rubbing the scalp with the middle bark of an elm tree, with water cress or even with onions followed by application of honey and boxwood. And today treatments recommended include the mange cure, creosote or cholesterol, but with perfume, quinine, resorcinol, tar and the constituents of the urine of the pregnant. May therapeutists of the future one day smile on present day concoctions with the same tolerance shown today to the treatments of the past.

It is not meant to imply from this that contemporaries and immediate predecessors of the present day physicians were content to rest on simply those measures. To be sure, such advances as have been made in physical therapy, endocrinology, physiologic chemistry and vitamin therapy have found their application to the problem of baldness, but with disheartening results. It was only a few years ago that ultraviolet ray therapy was held in high regard for ordinary baldness, but what temporary benefit was observed from it was probably due to the transient hypermia that was produced. In 1936 there was described a new method of treatment using the principle of vacuum pressure.[5] In treating older persons for peripheral vascular disease by means of vacuum pressure, it was observed that new hairs grew on legs that had previously been barren. The result was interpreted as a response to increased nourishment of the tissues, and on the assumption that baldness was due to follicular undernourishment, a special apparatus was devised to enable vacuum pressure treatment to the scalp. The results were reported to be satisfactory, for terminal hairs grew longer and thicker and were more pigmented; the regrowth extended up both temporal regions with closure of the bald pate, and the hair in general was said to have a luxuriant sheen. No mention was made of the time required to produce the results or of the permanency of the effect, and there were no illustrative photographs. The method, however, was immediately exploited. Vacuum pressure machines quickly found their way into many barber shops, and

4. Rolleston, J. D.: Dermatology and Folk Lore, Brit. J. Dermat. **52**:43 (Feb.); 73 (March) 1940.

5. Cueto, A. A.: A New Treatment for Baldness, Journal-Lancet **56**:571 (Nov.) 1936.

hope was reborn. But little is heard of the method today, and there have been no subsequent reports regarding it.

The stir created by endocrine therapy was even more spectacular, involving as it does one of the mysteries of medicine. Bengston,[6] in 1931, reported his results from treatment with pituitary (whole, anterior and posterior) of alopecia totalis in persons with obvious endocrinopathies, but in an addendum added the hopeful note that pituitary therapy apparently demonstrated greater primary stimulation of the hair follicle in the common types of baldness. Since the statement was based on an experience of but six weeks, he cautioned against enthusiasm for the treatment, but the newspapers failed to heed his advice and patients everywhere clamored for this type of therapy. Two years later, from experience gained from a larger group of cases, he again reported that the treatment gave results that were "interesting and suggestive, but not gratifying." Nevertheless, the attempt was continued, sometimes with the aid of other glandular products for their synergistic effects. Later,[7] eight years after introduction of this therapy, he was forced to accept the conclusion, based on the results in about 2,000 patients treated by 700 physicians in this country and abroad, that "pituitary, as it is,at present prepared, is of no practical value in alopecia prematura." There was one gratifying report, however, that of the Secretary of the Illinois State Board of Veterinary Examiners,[7a] who found that "pituitary injections stopped the habitual shedding of hair of several dogs."

Another interesting experiment was the effort to cure baldness by implanting fresh anterior lobes of pituitary glands of sheep into the subcutaneous tissue of the abdomen.[8] Fourteen men were so treated, and after seven months good results were noted in 4 of them and an increased growth of body hairs in 2 others. There was no mention made, however, in the report of the presence or absence of other signs of endocrine dysfunction, and I have watched in vain for a subsequent report of the permanency of the results.

Despite the universal failure so far of the method, pituitary substance is still being used in the treatment of baldness by some physicians, but not, I believe, by dermatologists, and it shall be to their everlasting credit that they were slow to adopt the method of pituitary therapy for ordinary baldness.

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6. Bengston, B. N.: Pituitary Therapy of Alopecia, J. A. M. A. **97**:1355 (Nov. 7) 1931.

7. Bengston, B. N.: Progress in Pituitary Therapy of Alopecia, Clin. Med. & Surg. **46**:5 (Jan.) 1939.

7a. Bengston, B. N.: Various Endocrine Extracts and Local Therapies in Alopecia, Clin. Med. & Surg. **41**:76 (Feb.) 1934.

8. Stanley, L. L., and Hawkins, J. O.: Implantations of Anterior Pituitary Glands in Alopecia, M. J. & Rec. **137**:462 (June 7) 1933.

Recently Goodman [9] suggested a sound basis for the use of the long-favored pilocarpine for the treatment of baldness. Pilocarpine, he pointed out, has an action on the sympathetic nervous system which is antagonistic to that of thallium acetate. Thallium acetate, which is thought to act through the sympathetic nervous system, when used for the treatment of tinea capitis produces in children a male pattern, the hippocratic type, of baldness. Goodman postulated, therefore, that hippocratic baldness is, in fact, a "pattern nerve baldness" and that any drug, such as pilocarpine, which acts on the sympathetic nervous system as a physiologic antagonist to thallium acetate might have a place in the treatment of ordinary baldness.

Various preparations of keratin, including hydrolyzed wool, have been suggested for the treatment of baldness, because a diet poor in protein has an adverse effect on the hair of animals. Its effect on human baldness has not been encouraging, however.

Another method suggested for the treatment of baldness, but not tried on a large scale, was that of injections into the scalp of a foreign protein, such as milk. My own experience with it in a few cases of alopecia areata was disappointing.

With the newer knowledge of vitamins it was inevitable that vitamin therapy be applied to the problem of baldness. A new compound,[10] inositol, which occurs naturally in the liver, in other animal tissues and in plants, has apparently been found useful for the prevention of baldness in rats. This development is a very recent one, and I know of no reports of its application to human baldness.

Even plastic surgery has been recommended for baldness. Okuda obtained good cosmetic results from tiny homotransplants, and Tauber,[11] in the Ceylon Branch of the *British Medical Journal*, recently claimed good results from full thickness grafts of hair-bearing areas from the sides and back of the head.

Finally, and very encouraging, is the account by Gill [12] in his "Black Magic and Men in White." He described several amazing drugs in the witchcraft-laden pharmacopeia of the Amazon jungle. Among these is one he has named avelina rosada; it is prepared from a fibrous root and has been used successfully since the days of the Incas as a dandrufficide, hair restorer and growth reactivator. Among the Indians who use it, he cites the thick lustrous tresses of the women, the unusual cleanliness, the absence of dandruff in both sexes and the universal lack

9. Goodman, H.: Pattern Nerve Baldness, M. Rec. **149**:9 (Jan. 4) 1939.

10. Woolley, D. W.: Nature of Anti-Alopecia Factor, Science **92**:384 (Oct. 25) 1940.

11. Tauber, H.: Alopecia Praematura and Its Surgical Treatment, J. Ceylon Br. Brit. M. A. **36**:237 (July) 1939.

12. Gill, R.: Black Magic and Men in White, Sat. Eve. Post **212**:18 (June 29) 1940.

of baldness as testimony of its value. Investigation of the drug in the United States, he reported, gave clinical evidence supporting in full all the claims of the jungle folk. This brings one right back to the beginning of the therapeutic cycle, which started with herbs, roots and plants and progressed through animal grease, invocations, vegetables, waste products, synthetic chemicals, foreign protein, artificial sunlight, suction on a vacuum, endocrine therapy, vitamin therapy and plastic surgery. The impressive list includes even desensitization therapy.[13] Despite the fact, however, that with baldness there are familial tendencies, and even seasonal variations, allergists have not yet claimed baldness for their domain.

EXPLANATIONS OF BALDNESS

Perhaps the most interesting chapter in the story of baldness is that dealing with the attempts to explain it. It is here that man's ingenuity is seen at its best, with the result that there is a long list of supposed causative factors for ordinary baldness, some based on fact, others seemingly logical and others again utterly fanciful. The following suggestion, for instance, was made:

> The various emotions to which the mind is subject act as directing causes for baldness; for, under the wearing exercise of thought, the nerve's supply to the hair follicle is cut off, the blood vessels receiving their nerve filaments from such sources become first dilated, then contracted, thus producing stagnation of the hair bulb. . . . Those who are concerned with the preservation of their hair should avoid all excesses or extraordinary excitement. They should shun mental and bodily overstimulation and endeavor to preserve an equable temperatment of mind and body . . . for fall of hair is often an indication of premature exhaustion of organic nervous energy.

As the phraseology indicates, this nervous exhaustion theory of baldness is quoted from a book published ninety years ago,[1] and it probably represents medical thought of many years before that. Today, although in modern word dress, there is a revival of the same old nervous exhaustion theory to account for diseases for which, unfortunately, there are no factual explanations. The trend is particularly strong in dermatology.

Then there was advanced the concept that baldness was caused by the overheating of the scalp from enlargment of its blood vessels. This was the result of a strong cardiac action, which in turn was caused by rich blood. The heart, it seemed, forced too great a quantity of blood into the scalp, enlarging and hardening the blood vessels, producing an abnormal amount of local heat, with consequent loss of hair, such as occurs from a fever. Nor was this action an independent one, for when the blood was rich, nervous energy was at a high pitch, and the ravages

13. Savill, A.: The Hair and Scalp, ed. 2, Baltimore, William Wood & Company, 1937.

of nervous energy have long been known. As proof of the theory witness the fact that strong hearts, nervous energy and baldness all become manifest in the prime of life. The main contribution of this theory apparently is that it is the bald-headed men who are the strong-hearted ones.

No less ludicrous is the suggestion that baldness is due to a toxin which develops in expired air when it is confined in a warm and moist space. These conditions are present in the upper part of the lungs, and persons who do not consciously breathe deeply to expand the upper part of their lungs become bald.

Still another amusing explanation for baldness is the so-called hair migration theory.[14] According to this theory, when hair falls from the scalp it reappears on another part of the body. One never wholly loses his hair; it simply migrates, for when the head goes barren the chest becomes fertile. It disappears from the scalp because there is a lack of metaphysical urge on the part of the scalp. If that urge is stimulated, hair will reappear where it is wanted. This theory offered recently as a new one was referred to almost one hundred years ago by Charles Dickens in an article titled, "Why Shave?" He raised the question "whether since what is gained in one place seems to be lost in another, the increased growth at the chin produced by constant shaving may not help to account for some part of the weakness of hair upon the crown." I suggest that if hair migrates at all, it does so only on a toupee, made from the hair of another man.

Hats, as a symbol of civilization, have long been accused of contributing to loss of hair. The conspicuous lack of baldness among full-blooded American Indians is said to be due to the custom of going without hats; yet in the Bodianus Manuscript, an actual Aztec text recently discovered in the Vatican library, there is reference to falling hair and treatment is recommended for it. Hats are thought to contribute to baldness in several ways: By their impermeability they exclude air and sunlight, and by their weight they compress the vessels of the scalp, which nourish the hair follicles.[15] As proof, it is cited that the hair first disappears from the part of the head where the circulation is weakest, that is, along the top, the region most remote from arterial force. The bald area gradually descends to the hat band area and there stops. The areas involved are those dependent on the temporal arteries for nourishment and seldom involve parts not exclusively dependent on the temporal and occipital arteries. These vessels lie on unyielding bone and are covered by thin tissue, a most favorable

14. Nessler, C.: Our Vanishing Hair, London, Alwyn Schmidt Publishing Company, 1853.

15. Dorsey, B.: Baldness, Cause and Prevention, Los Angeles, DeVorss & Company, 1939.

position for becoming compressed by hat bands. The temporal veins become enlarged and tortuous. This mechanism occurs particularly on a head whose broadest diameter is just in front of and behind the ears. The long, narrow head, flat at the sides and with no bulge, it is wrongly claimed, does not become bald. In that type of baldness in which a frontal patch of hair remains, it is said to be due to the presence of long supraorbital arteries which escape pressure from hat bands by passing over the forehead in slight concavities between the frontal eminences.

Hats are accused of contributing to baldness in still another way. Baldness, it is thought, is a manifestation of a transitional stage in man's evolution.[16] The general bareness of the human skin comes from the habit of wearing clothes. What little hair is now present is the vestige of a former abundant coat, for with civilization and domestication there is no longer need for hair. In the economy of nature, structures atrophy and even disappear when they cease to have a function, and the need of warmth and other protection afforded by hair is no longer important. Man's ancestor relied for protection of his head on a shock of hair. He now uses a hat, and as a result his shock of hair is gradually vanishing. McCarthy, however, has noted that in no country in the world do men wear hats so seldom as in Germany and yet in no other country are there so many bald men.

Some physicians believe that a lack of subcutaneous fat in the scalp is the cause of baldness. In the normal scalp there is a thick layer of subcutaneous fat, to which the skin is loosely attached and on which it is freely movable. In a hat-wearing man, consequent to the interference with its nutrition, the layer of fat gets thinner; the scalp becomes more firmly attached to the skull, and the skin becomes more tense. With these changes the hair becomes sparse, especially on the vertex, where pressure on the aponeurosis of the occipitofrontalis muscle is greatest. Thus, there is replacement of the subcutaneous fat by dense fibrous tissue, which by a process of induration causes atrophy of the hair follicles. Women are spared this misfortune because they have more subcutaneous fat and they do not lose it. Thus, actually it is the women who are the fat heads.

On the other hand, there are other physicians who would attribute baldness not to the absence of fatty tissue but to its presence; for the presence of fat under the skin compresses the follicles, causing them to atrophy, or it absorbs the nutriment, thereby, in a sense, starving the

16. Pusey, W. A.: Care of Skin and Hair, New York, D. Appleton and Company, 1929.

hair out, or, finally, the fat exercises an unfavorable effect on the sweat and sebaceous glands, thus indirectly affecting the hair.[17]

The striking fact that hippocratic baldness does not occur in women, children or eunuchs points directly to an endocrine factor in its production. The factor is probably in the nature of a lack of balance of the glands, and the glands which seem most important in the control of hair growth are the adrenals, the gonads, the thyroid and the pituitary.[18] The roughness and scantiness of the hair in cretinoid conditions, the abnormal growth of hair that often occurs in the presence of adrenal disease, the hair fall sometimes noticed after thyroidectomy, the increased growth in many acromegalic persons and the sexual distribution of hairs are all cited as evidence of an endocrine influence on the pilous system. The theories suggested to explain sexual differences in hair growth are, first, that the male type of hairiness is latent in all persons, but the ovary suppresses its development, and, second, hairiness of the male is really due to stimulation of testicular secretion, in the absence of which the body hair remains undeveloped. One must conclude with Danforth[17] that the evidences for an endocrine influence on the hair, though abundant, are difficult to interpret and that a practical knowledge of their mode of action is lacking. It would seem that sound policy should dictate that before advising hormonal therapy for simple baldness, there should be some other good evidence of endocrine dysfunction in the patient.

Sabouraud and his followers pointed out that 90 per cent of bald-headed men show evidence of seborrhoea oleosa with the presence of large numbers of microbacilli and that this is a most important factor in the production of baldness.[19] While they admitted that the causal connection lacks definite proof, the constant association is highly suggestive. In the usual case of baldness—though not necessarily in every case—the sequence of events is as follows: First, a noninflammatory branny scaling of the scalp appears, pityriasis simplex capitis, popularly called dandruff. After some years, in a majority of cases, a serous exudate develops on the scalp, giving to the scales an oil-like character, pityriasis steatoides. Then, with the onset of puberty there is excessive function of the sebaceous glands, seborrhoea oleosa, which interferes with growth and replacement of hair, leading to the end stage, alopecia. It is maintained that in both geographic pattern and sex relationship, premature alopecia, senile alopecia and the seborrheic form of baldness behave alike and that the three conditions therefore are regarded as different stages

17. Danforth, C. H.: Studies on Hair, Arch. Dermat. & Syph. **11**:494 (April); 637 (May); 804 (June) 1925; **12**:76 (July); 95 (Aug.); 380 (Sept.); 528 (Oct.) 1925.

18. Wigley, J. E. M.: Alopecia, Practitioner **142**:89 (Jan.) 1939.

19. McCarthy, L.: Diagnosis and Treatment of Diseases of the Hair, St. Louis, C. V. Mosby Company, 1940.

of the same disease, i. e., alopecia due to a micro-organism which acts in a seborrheic constitutional complex. In fact, Sabouraud and his followers were inclined to call ordinary baldness by the name seborrheic premature alopecia. Others, however, have noted that there are some men who do not become very bald despite a considerable amount of seborrhea for many years and that women with an equal amount of seborrhea rarely have the same amount of alopecia as do men. The fact, too, that baldness is generally confined to certain areas and may be associated with luxurious growth of hair on other parts of the scalp suggests to them that seborrhea is not the most significant factor in alopecia.[17]

German dermatologists apparently do not distinguish between seborrhea and pityriasis and attribute falling of hair to the abnormal cornification of the follicle and the development of parakeratosis. This occurs especially when there is abnormal metabolism of cholesterol, with consequent decreased content of cholesterol in sebaceous gland secretions. Though they reported good results from rubbing cholesterol into the scalp, Sabouraud gave this type of therapy a good trial without notable success.[18]

The influence of heredity as a significant factor in baldness long has been recognized. Of all the theories, heredity, more than any other, offers an explanation for the differential sex incidence of baldness. Osborn,[20] who studied twenty-two families into the fourth and fifth generations, observed that baldness was inherited as a sex-limited trait, dominant in men and recessive in women, and that it was directly inherited from father or mother to son, even though the mother herself was not bald. She observed, too, that a man who did not show baldness himself did not transmit it to his children. Baldness appeared in women only when the inheritance was duplex, thus explaining the rarity of baldness in women but also explaining the few existing cases. When a woman inherited the simplex condition, she did not become bald herself but transmitted baldness in the long run to half of her sons, and also possibly to half of her daughters. A bald man with simplex inheritance transmitted baldness in the same manner.

It is held by some students that in bald-headed persons it is not the alopecia itself but the shape of the head that is inherited and that from wearing hats the consequent pressure on the blood vessels supplying the scalp causes the loss of hair. One case studied by Osborn would seem to contradict this. It is the case of a man who, very bald before the age of 30, had an only son who had an exact bald pattern at birth, with hair in fringes above the ears and at the back. Later, the son's hair grew and became normal in appearance, but at the age of 19 he had a prominent forehead. In this case certainly it would seem that it was

20. Osborn, D.: Inheritance of Baldness, J. Heredity **7**:347, 1916.

the pattern of baldness rather than the shape of the head that was inherited. One woman who had been married twice, each time to a man with hair, had a bald son by each. In this case the inheritance was shown to be transmitted from her mother. In general, Osborn found that baldness was a segregating character which affected some members of a family but not all unless it came from both sides of the

Ordinary baldness (Miller [21]). (Any resemblance to persons in the audience is entirely coincidental.)

ancestry. Apparently in the cases that Osborn studied alopecia occurred regardless of whether the hair was thin, normal or heavy, but in general when the hair was very heavy in youth, usually baldness did not develop. Two families, incidentally, with exceptionally heavy hair, were traced into four generations, and in these families there was no baldness despite the wearing of hats and poor general health in some of the members.

Perhaps the most interesting of all the explanations put forth to account for baldness is that of Gerritt S. Miller Jr.,[21] curator, Division of Mammals, United States National Museum, Washington, D. C. Miller pointed out that all of the usual explanations for baldness fail to take into consideration the zoologic possibility that baldness may be a generalized primate trait instead of a specifically human development and that it is forced on man because it is one of the traits that are common property of the primates, the animal group to which man belongs. Baldness, according to this view, should be explained in terms of the great heritage of characteristics that man shares with all his primate relatives, and patterning is one of the characteristics. Patterning is apparently physiologically inherent in all animals and consists in the arrangement of contrasted colored areas on the surface of the body or variously sized outgrowths, or both combinations of colors and outgrowths. The color markings of a butterfly are examples of patterning. In primates, according to Miller, patterning is conspicuously developed on the head, and although the human head pattern is not exactly duplicated by other primates, all the elements that enter into it can be found easily in nonhuman members of the order. This is particularly true of the various types of baldness that afflict men, and with photographs Miller illustrated baldness in monkeys that is similar to that in man. The uniform raising of the forehead line has its parallel on the head of a certain South American monkey. Similarly, the temporal wedges, the bald pate and the hippocratic type of baldness have almost exact counterparts in other primates. Man, therefore, is bald because as a primate he cannot avoid it, for it is imposed on him by his primate heritage.

It would be interesting to know whether the bald monkeys are the intellects in their set or whether they are held up to ridicule. Are they the strong hearted? Do they breathe impure air? Or does their hair merely migrate? Do they have seborrhoea oleosa? Or is it that they suffer from nervous exhaustion because of the heightened tempo of their way of life?

CONCLUSION

The man who would avoid baldness had better use greater care in the choice of his ancestors, for "There's no time for a man to recover his hair that grows bald by nature" (Shakespeare).

25 East Washington Street.

21. Miller, G. S., Jr.: Human Hair and Primate Patterning, Smithsonian Misc. Collect. **85**:10 (Dec.) 1931.

SQUAMOUS CELL EPITHELIOMA ASSOCIATED WITH SENILE KERATOSIS ON THE LEG OF A NEGRO

REPORT OF A CASE

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The following case is reported because of the unusual coincidence of the following factors: the development of a squamous cell epithelioma on the leg, its occurrence in a highly pigmented Negro and its association with senile keratosis, from which it probably arose.

REPORT OF CASE

L. H., a 73 year old dark-skinned Negress, entered the outpatient department of the Harlem Hospital because of a lesion on the leg which would not heal in spite of numerous local applications. The abnormality first appeared about two years previously as a pea-sized scaly lesion and gradually progressed in size. It was painless and bled readily on the slightest trauma.

Examination showed on the anterior surface of the upper third of the right leg a round granulomatous lesion about the size of a 25 cent piece. It was elevated ½ inch (1.3 cm.) above the surface of the skin (fig. 1). On the anterior aspect of the same leg there were several pea-sized papulosquamous lesions, one of which was situated about 1 inch (2.5 cm.) from the large lesion. On the anterior surface of both legs there was a reticulated pigmentary disturbance characterized by discrete and confluent depigmented pinhead-sized to pea-sized macules, giving a salt and pepper appearance to the leg. According to the patient's history, the pigmentary disturbance had preceded the elevated lesion by several years.

On the left leg there were a few senile keratoses as well as reticulated depigmentation. The rest of the examination gave negative results. There was no inguinal adenopathy. The urine was normal, and the Wassermann reaction of the blood was negative.

The diagnoses which were considered included syphilis, granuloma pyogenicum, a drug eruption and a malignant condition. In the absence of a history of syphilis and with normal physical and serologic findings, syphilis was ruled out. There was no history of the use of drugs which would suggest the diagnosis of a drug eruption. The final diagnosis therefore remained between granuloma pyogenicum and a malignant condition.

A biopsy specimen was taken from the granulomatous plaque and from one of the satellite papulosquamous lesions.

Histologic examination of the papulosquamous lesion showed the following picture (fig. 2): In the epidermis there was dense hyperkeratosis with moderate

From the dermatologic clinic of the Harlem Hospital, service of Drs. S. Irgang and E. R. Alexander.

Fig. 1.—Granulomatous lesion with a satellite papulosquamous lesion at the right. Note the reticulated depigmentation.

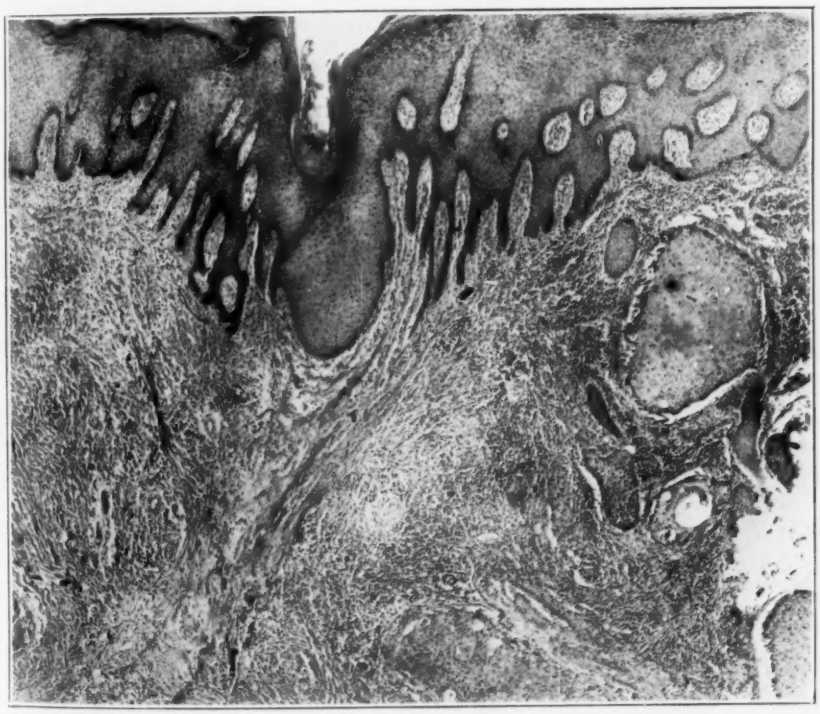

Fig. 2.—Squamous cell epithelioma; photomicrograph showing hypertrophied and hyperkeratotic epidermis with elongation and anastomosis of the rete pegs, intact palisade layer and whorl and pearl formation infiltrating the cutis en masse.

acanthosis and irregular elongation of the rete pegs, some of which extended almost to the midcutis. In the rete pegs there were several anaplastic cells, each consisting of a large round cell body with increased protoplasm and a hyperchromatic nucleus undergoing mitosis. In the cutis the papillary bodies were elongated and enlarged, with nonspecific cellular infiltration and capillary dilatation. The pigment was almost entirely absent in the basal cells, an unusual factor for hyperpigmented skin. In short, there was a tendency toward invasion of the cutis by the epidermis with evidence of anaplasia and senile keratosis with precancerous process.

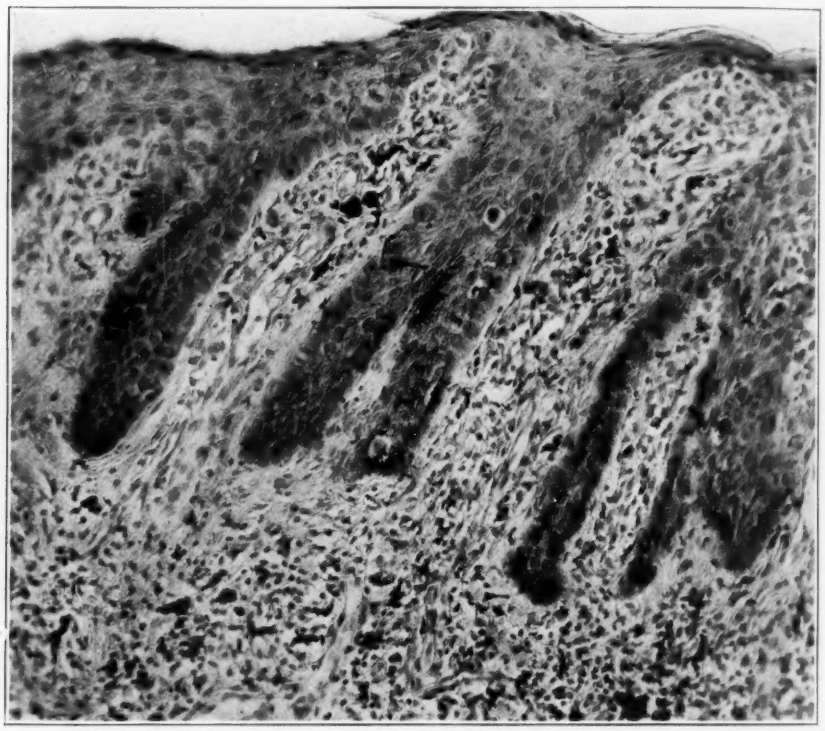

Fig. 3.—Senile keratosis; photomicrograph showing moderate acanthosis with elongated rete pegs invading the midportion of the cutis. In the central peg are several anaplastic cells with large hyperchromatic nuclei. The pigment is washed out of the basal cell layer into the cutis.

In one portion of the section from the large lesion there were features similar to those aforementioned in the senile keratotic lesion, i. e., hypertrophied and hyperkeratotic epidermis with no pigment invading the cutis. Further in the section (fig. 3) one could observe dense hyperkeratosis with hyperplasia of the prickle cell layer. There was anastomosis of the rete pegs which extended downward beyond the upper part of the cutis. The palisade cells of the basal layer remained intact. In the midportion of the cutis were seen parts of the digital projection of the hyperplastic epidermis with whorl and pearl formation, in short, squamous cell epithelioma infiltrating en masse.

COMMENT

It is an accepted opinion that senile keratosis gives rise to malignant degeneration nearly always of the prickle cell type. This opinion is substantiated by the evidence presented in figure *2*, where the senile keratotic process shows anaplastic cells and a tendency to invade the cutis.

Since senile keratosis is extremely rare in highly pigmented persons and is more prevalent in light-colored persons, e. g., blonds, it follows that one may be dealing with an inhibiting factor, such as pigment. In this case depigmentation preceded the lesions, which were histologically almost entirely free of pigment. It is therefore possible that dark pigment may act as a protection against the formation of precancerous and epitheliomatous growths.

In a review [1] of 5,000 cases of diseases observed at Harlem Hospital, where the patients are nearly all Negroes, only 1 case of basal cell epithelioma was found; the patient was a mulatto and the growth occurred on the nose.

SUMMARY

A case is reported of a dark-skinned Negress with depigmentation on the legs on which senile keratosis and squamous cell epithelioma had developed. The diagnosis was proved by histologic examination. It is suggested that the disappearance of pigment may have acted as a contributing factor in the development of the malignant growth.

2135 Seventh Avenue.

1. Fox, H., in discussion on Hopkins, R., and Van Studdiford, M. T.: Multiple Epithelioma and Pigmentary Dermatoses in a Negro Boy, Arch. Dermat. & Syph. **29**:408 (March) 1934.

CONTACT DERMATITIS DUE TO UNDERWEAR

OBSERVATIONS IN FOURTEEN CASES WITH SUMMARY OF EFFORTS TO DISCOVER THE CAUSE

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AND
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Fourteen patients with contact dermatitis were admitted to the dermatologic service at the St. Louis City Hospital from May 1940 to December 1940. This dermatitis was caused by the wearing of new unwashed shorts purchased at chain department stores. All the patients were male adolescents; they had worn the shorts for at least forty-eight hours prior to the appearance of a sharply demarcated dermatitis covering the lower part of the back, the buttocks and the upper parts of the thighs. Vesiculation was never noted. Edema with associated pain and pruritus about the genitalia was a constant feature. In several cases catheterization was necessary. In no case could a history of previous sensitization be elicited. All the patients were comparatively free from toxic symptoms after the first few days. In 1 case infection was superimposed on the penile edema.

Response to treatment was poor. Several patients retained a pruritic erythema after four weeks' treatment.

REPORT OF TYPICAL CASES

CASE 1.—J. F., a white boy, was admitted on Oct. 11, 1940, with a swelling of the scrotum and penis and a pruritic erythematous papular dermatitis on the buttocks and thighs sharply limited to the area covered by shorts, which were purchased on October 7 from a chain department store and worn at once without washing. On October 9 the patient began to notice small pruritic papules which were confined to the area covered by the new underwear, with edema of the genitalia. The edematous area had been bathed with solution of sodium bicarbonate, and an unidentified proprietary ointment also had been used. The condition became worse, and the patient was admitted to the hospital. The patient was in good health except for the dermatologic manifestations. A papular erythematous eruption was noticed on the abdomen and thighs sharply limited to the area covered by the shorts, with an associated inguinal adenopathy. The penis and scrotum were reddened and edematous. A patch test with the underwear cloth

From the St. Louis City Hospital, Unit 2 (Department of Dermatology, St. Louis University School of Medicine), service of Dr. Joseph Grindon Sr.

elicited a positive reaction. The edema of the scrotum and the penis soon receded under local treatment, but the pruritic erythematous dermatitis persisted. The patient was discharged on October 18 and was treated in the outpatient clinic with various "shake" mixtures until October 30. When last seen, three weeks later, the patient still had a scaly pruritic dermatitis.

CASE 2.—H. B., a white boy aged 15, was admitted on Oct. 17, 1940, with severe pruritus and edema of the scrotum and penis of four days' duration. The symptoms had appeared three days after he wore new underwear. The physical examination gave essentially negative results except for the dermatologic manifestations. Wherever the underwear had come in contact with the skin, there was an erythematous dermatitis involving the lower portion of the abdomen and the upper parts of the thighs. A decided edema of the genitalia was noticed. A patch test with the underwear cloth elicited a strong reaction. The edema of the scrotum and penis subsided under local treatment. On October 23 only the pruritic

Fig. 1 (patient J. G.).—Typical moderate edema of the penis in patient with contact dermatitis due to underwear.

erythematous area remained. The patient was discharged, and boric acid and 2 per cent resorcinol lotion was prescribed for use at home. A scaly pruritic desquamation remained one month later.

INVESTIGATION OF THE CAUSE OF THE DERMATITIS

Early in our study of these cases we noticed that patch tests with the unwashed material elicited positive reactions but that tests with similar material which had been laundered gave negative results. We were thus led to believe that the causative factor of this dermatitis might be found in the substance removed from the cloth by washing.

In March 1940 Dr. D. S. Mitchell, of Montreal, Canada, reported that in Canada there were many cases of dermatitis in persons wearing cotton fabrics finished with an American-made preparation. Schwartz

and others [1] recently focused attention on dermatitis caused by the new resin fabric finishes. These investigators suggested that the oleoresin in the textile finish was the cause of this dermatitis. They also suggested that the abietic acid which is present in these oleoresins is the direct causative agent. It has been stated that abietic acid is a cause of adhesive tape dermatitis in hypersensitive persons.[2] Following these suggestions we began a study of this contact dermatitis.

Method.—Cooperative patients in the St. Louis City Hospital were used as test subjects. The patients were chosen at random from all wards. Men, women and children of varied ages were tested. Dilutions of the various constituents [3] of the filler were made in percentages roughly estimated to be those to which the patient might be exposed on wearing the apparel. Obviously these concentrations would vary with the degree of perspiration and bodily cleanliness. The skin was not prepared or cleansed. Small pieces of gauze were moistened with dilutions of the various materials. The oily substances were applied directly to the skin. The gauze pledgets and the oily materials were covered with cellophane and then bound in place with adhesive tape squares, which assured close contact with the skin. The back was chosen as the test site rather than the thigh; this reduced to a minimum the factor of scratching or tampering with the patches on the part of the patient. The patches were removed and the reactions tabulated in from forty-eight to one hundred and forty hours.

Three groups of persons were tested. Those in group 1, consisting of 95 persons, were tested with the various dilutions of the oleoresin in an alcoholic solution. The dilutions were 33.3, 3.33, 0.333 and 0.033 per cent. These 95 persons were also tested with cotton cloth impregnated solely with a 1.98 per cent solution of the oleoresin and with the finished cloth which was thought to cause the original dermatitis. Other substances tested in group 1 were 0.015 per cent bluing, 0.7 per cent sulfonated coconut oil and 5 and 0.5 per cent sulfonated tallow.

Each member of group 2, consisting of 81 patients, was tested with five dilutions of abietic acid in an alcoholic solution. These five dilutions were 1:1,000,000, 1:100,000, 1:10,000, 1:1,000 and 1:100. Also tested in this group were 1:1,000 and 1:100 dilutions of the synthetic wetting-out material (which is an aqueous paste of a sulfonated salt) and normal potato starch in dilutions of 1:1,000 and 1:100.

Each member of group 3, consisting of 58 persons, was tested with five dilutions of abietic acid in a solution of liquid petrolatum. These five dilutions were 1:1,000,000, 1:100,000, 1:10,000, 1:1,000 and 1:100. We also tested with 1:1,000 and 1:100 eqeuous dilutions of sour potato starch and 5 and 0.5 per cent rancid sulfonated tallow.

The reactions in test group 1 were read after five days. Those in test groups 2 and 3 were read after two days.

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1. Schwartz, L., and others: An Outbreak of Dermatitis from New Resin Fabric Finishes, J. A. M. A. **115**:906-911 (Sept. 14) 1940.

2. Schwartz, L., and Tulipan, L.: Text-Book of Occupational Diseases of the Skin, Philadelphia, Lea & Febiger, 1939, pp. 111 and 354.

3. The constituents of the filler and the cloth used were obtained from the original manufacturers. The chemical composition and formulas of many of these "trade name" substances are not available.

Results.—Of the 95 persons tested in group 1 there were positive reactions in 13 subjects with the 33.3 per cent dilution of the oleoresin, in 6 with the 3.33 per cent dilution, in 8 with the 0.333 per cent dilution and in 2 with the 0.033 per cent dilution (table 1). Tests with the finished cloth elicited positive reactions in 6 subjects, and the oleoresin-pregnated cloth, in only 2 subjects. Tests with the 0.015 per cent bluing, 0.7 per cent sulfonated coconut oil and the 5 and 0.5

TABLE 1.—*Results of Patch Tests with Oleoresin, Oleoresin-Filled Cloth, Finished Cloth, Bluing, Sulfonated Coconut Oil and Sulfonated Tallow in Ninety-Five Persons*

	Positive	Negative	Percentage Positive
Oleoresin, 33.3 per cent	13	82	13.6
3.33 per cent	6	89	6.3
0.333 per cent	8	87	8.4
0.033 per cent	2	93	2.1
Sulfonated coconut oil, 0.7 per cent	0	95	0
Oleoresin-filled cloth, 1.98 per cent	2	93	2.1
Finished cloth	7	88	7.3
Bluing, 0.01 per cent	0	95	0
Sulfonated tallow, 5 per cent	0	95	0
0.5 per cent	0	95	0

TABLE 2.—*Results of Patch Tests with Abietic Acid in Alcoholic Solution, a Synthetic Wetting-Out Agent and Fresh Starch in Eighty-One Persons*

	Positive	Negative	Questionable	Percentage Positive
Abietic acid, 1:1,000,000	0	81	0	0
1:100,000	0	81	0	0
1:10,000	0	76	5	0
1:1,000	0	75	6	0
1:100	0	67	14	0
Synthetic wetting-out agent, 1:1,000	0	81	0	0
1:100	0	81	0	0
Fresh starch, 1:1,000	0	81	0	0
1:100	0	81	0	0
Ninety-five per cent alcohol	0	81	0	0

per cent sulfonated tallow elicited no reactions. Eleven patients who had ten days previously showed no reactions were tested in order to determine whether sensitization had developed. Two of these gave positive reactions with a 33.3 per cent dilution of the oleoresin.

In the second group, 81 subjects tested with the various dilutions of abietic acid in an alcoholic aqueous solution, there were no positive reactions; however, there were a number of questionable reactions which have been tabulated (table 2). Patch tests with the synthetic wetting-out material in dilutions of 1 : 1,000 and 1 : 100, normal starch in dilutions of

1 : 1,000 and 1 : 100 and 95 per cent alcohol elicited no positive reactions. Eleven patients in this group were retested ten days later for sensitization with the same materials. These patients gave no reactions.

Fig. 2 (patient H. J.).—Positive reactions to patch tests with (*1*) a moderate dilution of oleoresin, (*2*) oleoresin-filled cloth and (*3*) original unwashed shorts.

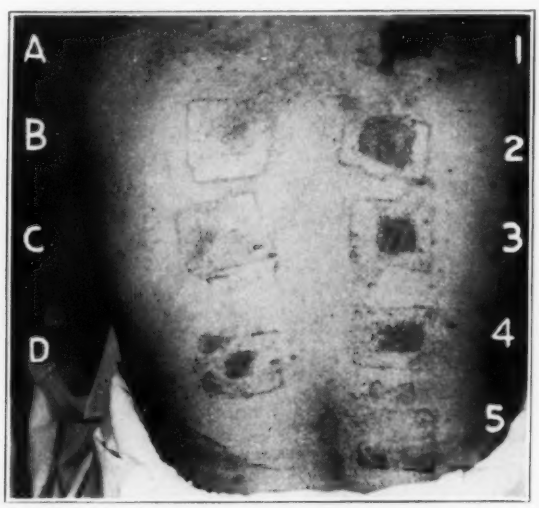

Fig. 3 (subject B. D.).—Reactions to patch tests with (*A*) 1 : 100 abietic acid (negative), (*B*) 1 : 1,000 abietic acid (negative), (*C*) 1 : 10,000 abietic acid (negative), (*D*) oleoresin-filled cloth (positive), (*1*) 33.3 per cent oleoresin (positive), (*2*) 3.33 per cent oleoresin (positive), (*3*) 0.333 per cent oleoresin (positive), (*4*) 0.033 per cent oleoresin (positive) and (*5*) adhesive tape control (negative).

Test group 3, consisting of 58 persons, was largely used as a check group on test group 2 (table 3). Abietic acid was placed in a liquid petrolatum U. S. P. solution instead of in an alcoholic solution. Starch

was made sour by incubating it for ninety-six hours, and rancid sulfonated tallow was used. Patch tests with abietic acid solutions in liquid petrolatum and with the sour potato starch solutions elicited no positive reactions. We have noted in the table the few questionable reactions to abietic acid. Patch tests with the rancid sulfonated tallow in 5 and 0.5 per cent solutions elicited a positive reaction in 1 person. In 45 of these subjects tests with adhesive tape elicited reactions varying

TABLE 3.—*Results of Patch Tests with Abietic Acid in Liquid Petrolatum, Sour Potato Starch, Rancid Sulfonated Tallow, Liquid Petrolatum and Adhesive Tape in Fifty-Eight Persons*

	Positive	Negative	Questionable	Percentage Positive
Abietic acid, 1:1,000,000	0	57	1	0
1:100,000	0	57	1	0
1:10,000	0	54	4	0
1:1,000	0	55	3	0
1:100	0	56	2	0
Rancid sulfonated tallow, 5 per cent	1	57	0	1.7
0.5 per cent	1	57	0	1.7
Potato starch, 0.7 per cent	0	58	0	0
Liquid petrolatum	0	58	0	0
Adhesive tape	45*	13	0	77.0

* In 5 of the 45 persons with reactions to adhesive tape the reactions were vesicular.

TABLE 4.—*Results of Patch Tests with Abietic Acid, Oleoresin and Oleoresin-Impregnated Cloth in Four Patients Who Had Been Treated for Underwear Dermatitis*

	Patient			
Substances Tested	R. S.	H. H.	C. L.	M. D.
Abietic acid, 1.1,000,000	—	—	—	—
1:100,000	—	—	—	—
1:10,000	—	—	—	—
1:1,000	—	—	—	—
1:100	—	—	—	—
Oleoresin, 33.3 per cent	+	+	+	+
3.33 per cent	+	+	+	+
0.333 per cent	+	+	+	+
0.033 per cent	+	±	±	±
Oleoresin cloth	+	+	+	0

from a slight erythema to vesiculation. Five of these 45 reactors showed vesiculation.

Four of the 14 patients with contact dermatitis were given patch tests with the various dilutions of abietic acid and of oleoresin (table 4). Vivid reactions were obtained with the stronger dilutions of the oleoresin. One of the 4 patients gave a positive reaction to the weakest dilution, 0.033 per cent, of oleoresin, and the other 3 gave questionable reactions to this dilution. None of the 4 patients gave the slightest reaction to any of the dilutions of abietic acid.

COMMENT

We were greatly interested in the reactions to patch tests with abietic acid, because it has been suggested by other investigators that some persons with dermatitis may have been sensitized previously by abietic acid, which is contained in the resin backing of some adhesive tapes.[1] Our results seem to show that abietic acid is apparently an inactive constituent of resins, insofar as contact dermatitis is concerned. We did not find it to be one of the sensitizing agents contained in adhesive tape.[4]

The abietic acid which we used for patch tests was obtained from a commercial company and represents a commercial grade. It probably contains pimaric and pyroabietic acid in considerable amounts. The neutral equivalent of the acid used was found to be 315 to 320; the melting point was 120 to 125 C. Pure abietic acid should melt at 170 to 175 C. Abietic acid is not soluble in water.

We have noted the apparent discrepancy in the results of testing with finished cloth and plain cotton cloth impregnated with 1.98 per cent oleoresins. It is possible that the variation is due to the different physical properties of the two cloths. The oleoresin-impregnated cloth, when applied as a patch, absorbs water with difficulty, while the finished cloth which has been processed readily absorbs water. A much better contact with the skin is thus obtained with the finished cloth.

Starch is an essential part of nearly all cloth finish. It occurred to us that since large vats of finish are made up and allowed to stand for periods of time, breakdown products of starch might cause dermatitis. Patch tests with neither normal potato starch nor incubated potato starch elicited positive reactions.

It may likewise be said for the oily products which go into this finish that apparently rancidity may have some deleterious effect; however, our results are not conclusive.

SUMMARY AND CONCLUSIONS

In 14 cases of underwear dermatitis the condition was caused by the commercial oleoresin used in the cloth finish.

According to the results we obtained from 695 patch tests on 139 persons, abietic acid is apparently not the basic agent causing underwear dermatitis. Our investigations showed that it has little or no relation to adhesive tape dermatitis.

The commercial oleoresin sensitizes in high concentration, but abietic acid does not.

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4. Schwartz, L., and Peck, S. M.: The Irritants in Adhesive Plaster, Pub. Health Rep. **50**:811-819 (June 14) 1935.

Patch tests with normal potato starch, sour potato starch, bluing, synthetic wetting-out material and sulfonated coconut oil as used in the textile industry elicited no positive reactions in our series.

Patch tests with normal sulfonated tallow elicited no reaction, but tests with rancid sulfonated tallow in the dilutions used in this experiment gave 1 reaction.

Dr. William G. Coleman supplied aid and suggestions, and Miss Jane Rhein gave technical assistance.

TOPICAL TREATMENT WITH SULFATHIAZOLE

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AND
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Acceptable methods for the treatment of common diseases, such as impetigo and related ecthyma and pyoderma, are numerous. The successful management in individual cases, however, is at times difficult, and a desire for improvement is indicated by the frequency with which new methods are proposed. The most widely used drug in the United States is ammoniated mercury, applied usually in the form of an ointment. In many cases it gives excellent results. It has, however, definite limitations. It is prone to produce contact dermatitis in a fairly high number of patients; moreover, it is at times difficult to apply this medication in ointment form to a moist surface, such as is frequently presented in impetigo and in ecthymatous ulcers. This is particularly true when crusts are removed in the office and treatment is immediately applied. These same objections hold true with less commonly used medications, such as resorcinol, sulfur and a number of the proprietary mercurial preparations. Gentian violet, in the usual 2 per cent aqueous solution, or even stronger, has been extensively used within the past ten years. It has the disadvantage of being dirty, but only rarely does it cause an eczematous irritation. Recently, however, it has been reported as causing an ulcerative reaction when used in the treatment of impetigo.[1] We have recently had the opportunity of observing this reaction when using the drug in treating uncomplicated impetiginous lesions on the face. Such results are of course most undesirable. Silver nitrate solution (5 to 10 per cent) has been one of our favorite methods of treatment, but it is difficult to use and its application is painful and disfiguring. There is certainly room, we believe, for improvement in methods of local treatment.

The evaluation of any new method of treatment must rest in its comparison with the treatment already accepted. Sulzberger[2] stated that under proper management and in the absence of any complicating

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From the Department of Dermatology and Syphilology, Dade County Hospital, Kendall, Fla.

1. Goldman, L.: Ulcerative Reaction from Gentian Violet in the Treatment of Impetigo Contagiosa, Arch. Dermat. & Syph. **42**:1122 (Dec.) 1940.

2. Sulzberger, M. B., and Wolf, J.: Dermatologic Therapy, Chicago, The Year Book Publishers, Inc., 1940.

dermatitis, ordinary impetigo may be cured in from five to twenty-five days. Pratt, Imhoff and Decker [3] reported a new method, the use of ammoniated mercury in a colloidal kaolin lotion, which required an average of fifteen days for cure, as compared with ammoniated mercury ointment, which required an average of twenty-six days. Obviously, it is difficult to compare any methods of treatment on the basis of time required for cure, except with a large series of cases. The severity of the dermatitis, the variations among persons and the thoroughness with which the prescribed treatment is used make a tremendous amount of difference in the results obtained. For ecthyma and pyogenic ulcers of various types on the lower extremities, no method of treatment has proved particularly valuable. Adjuvant treatment with roentgen rays, tonics for improvement of the general health and instructions as to an adequate diet, which are included in a discussion of treatment, serve only to indicate that therapeutic results with topical applications have at times been far from satisfactory. In treating patients from a county hospital, comprising persons in a low income group whose personal hygiene, diet and general health are not of the best, we have encountered persistent difficulties.

In view of these considerations, we have deemed it worth while to report a method of treatment which has been found almost uniformly satisfactory. The time required for care, the simplicity of application and the freedom from complicating reactions all recommend the further use of sulfanilamide and its derivatives as topical medications.

The British literature contains many reports of the local use of these compounds in the successful treatment of open wounds of all types. MacKenna [4] mentioned the successful treatment of ecthyma and impetigo contagiosa with sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) in powder form. Spink and Paine [5] used sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) in powder form, in a 1 per cent aqueous solution and suspended in cod liver oil in the local treatment of staphylococcic infections of various types and reported the method efficient. Sulfanilamide in a 4 per cent ointment was recommended by Brunsting [6] for the treatment of impetigo contagiosa. Herrell and

3. Pratt, A. G.; Imhoff, R. E., and Decker, H. B.: Impetigo Contagiosa Treated with Ammoniated Mercury-Colloidal Kaolin Lotion, J. M. Soc. New Jersey **36**:442 (July) 1939.

4. MacKenna, R. M. B.: Local Treatment with Sulphonamides, Brit. M. J. **2**: 99 (July 20) 1940.

5. Spink, W. W., and Paine, J. R.: Local Use of Sulfathiazol in Treatment of Staphylococcic Infections, Minnesota Med. **23**:615 (Sept.) 1940.

6. Brunsting, L. A.: Treatment of Common Diseases of the Skin, Journal-Lancet **60**:438 (Oct.) 1940.

Brown [7] used sulfanilamide and some of its derivatives in suspension or in powder form in 21 cases of varying types of wounds and postoperative infections. Beneficial results were observed in most of the cases.

In the present series sulfathiazole has been used both as a powder and in an ointment. The drug in the ointment has varied in concentration from 5 to 25 per cent, and it has been incorporated in various types of pastes and ointments prescribed to suit the presenting dermatitis. At the Dade County Hospital a 10 per cent concentration of sulfathiazole in cod liver oil ointment was given routinely for local application. No specific instructions were given, except that the crusts were to be removed, preferably with soap and water, and the ointment was to be applied twice daily. In many cases the use of soap and water was omitted, or they were used only indifferently. In private patients the treatment was initiated by removal of the crusts and opening of the blisters during the first office visit. Sulfathiazole powder was blown onto the moist lesion, and the patient was instructed to remove twice daily the crust which would form. This was done by applying the prescribed ointment, containing from 10 to 20 per cent sulfathiazole, to the crust for several hours. When soft, the crust was removed with soap and water and the powder again used. For home use, the patient was instructed to apply a small amount of the powder with a cotton applicator or toothpick, covering only moist areas.

REPORT OF CASES

CASE 1.—H. B., a 12 year old Negress, was first admitted to the Dade County Hospital on Nov. 11, 1939, with a diagnosis of acute sinusitis. Later a staphylococcic pyelitis and septicemia developed. Examination at the time of admission showed several scattered large purulent crusted lesions on both shins. The general treatment included multiple transfusions of blood and intravenous administration of neoarsphenamine, metaphen and gentian violet. The patient was discharged from the hospital on Jan. 24, 1940 and was well except that the ulcers on the legs persisted. During the next ten months local treatment was administered from time to time to the ulcers on the legs, without effect. On November 14 a cod liver oil ointment containing 10 per cent sulfathiazole was prescribed, to be applied twice daily. One week later the purulent ulcers were healed for the first time in twelve months.

CASE 2.—W. C. A., a 13 month old Negro girl, was seen at the hospital with a generalized purulent crusted dermatitis of three weeks' duration. She was reported to have had infantile eczema for five months and to have suffered from a recent exacerbation. A cod liver oil ointment containing 10 per cent sulfathiazole was applied twice daily to the areas of pyoderma. In one week the patient returned, presenting only an eczematoid dermatitis and no infection. Examination of the

7. Herrell, W. E., and Brown, A. E.: Local Use of Sulfamido Compounds in the Treatment of Infected Wounds, Proc. Staff Meet., Mayo Clin. **15**:611 (Sept. 25) 1940.

blood, after generalized application of the aforementioned preparation for one week, showed no sulfathiazole. This treatment was discontinued, and a tar paste was used. Further improvement was not obtained from local treatment, and the secondary infection recurred the following week.

To date 53 patients have been treated by this method. Our results may be grouped and summarized as follows: Thirty-three patients with impetigo, varying in duration from two to twenty-one days, were observed or reported to be well in from four to ten days (average one week). Twelve patients with ecthyma, varying in duration from two weeks to twelve months, were clear of secondary infection within one week. Additional time, however, was required for complete healing. The remaining patients with secondarily infected dermatoses gave an immediate response so far as the secondary infection was concerned but without much change occurring in the underlying dermatitis. The local use of sulfathiazole has been effective in the control of the infectious element in a wide variety of dermatoses.

We have as yet observed no instance in which there has been any deleterious effects on the skin from the local application of sulfathiazole. Specific sensitization of the contact type has not been observed during the two month period that we have used the treatment. An unsuccessful attempt to demonstrate sulfathiazole in the blood after generalized application of an ointment to an exudative dermatitis was made (case 2). The method used was that described by Bratton and Marshall and modified by M. Bodansky.[8] If subsequent determinations of the level in the blood demonstrate that sulfathiazole is not absorbed when applied locally, it will not be necessary to consider the usual contraindications for the use of such a medication. We feel that the beneficial action of the drug occurred locally in the tissue and was not a systemic response in the cases presented. We do not suggest that the drug acts directly on the infecting organism, but we believe that it is likely that some local tissue response occurs. Herrell and Brown [7] showed concentrations as high as 2.5 to 3 mg. per hundred cubic centimeters of blood in patients receiving sulfanilamide locally in infected thoracic cavities. They offered the opinion that only the skin over body cavities, with large surfaces, will absorb a sufficient amount of the drug to show a systemic response. Apparently it will not be necessary to be concerned with the possibility of a systemic reaction. No tendency to retard healing has been observed; in fact, the reverse seems to be true, namely, that healing is accelerated.

SUMMARY

Fifty-three patients with various cutaneous infections, chiefly impetigo and ecthyma, have been favorably treated by the local application of

8. Bodansky, M.: Tech. Bull. Registry M. Technology, November 1940, p. 151.

sulfathiazole powder and sulfathiazole in an ointment base. No detrimental local or systemic effects have been observed. This method of treatment has proved to be more efficacious than others that we have used. Its effectiveness and the ease of application should recommend it for a more extensive therapeutic trial.

NOTE.—Since this paper was accepted for publication a case has been observed by one of us (L. C.) in which local sensitivity to sulfathiazole powder probably exists. Insufflation of powdered sulfathiazole into the external auditory canals to control secondary infection in a case of chronic, eczematous dermatitis was followed by an acute exacerbation. After a period in which only palliative therapy was used, the powder was again insufflated into one ear, with a prompt recurrence of acute dermatitis, while the condition in the other ear, which was untreated, remained chronic. The reaction to patch test with sulfathiazole powder on the forearm was negative after forty-eight hours. Approximately six weeks after the last clinical test the patient was given 15 grains (1 Gm.) of sulfathiazole by mouth. Four hours later edema of the ears was noted; in a short time an acute dermatitis with massive edema of the face and ears resulted, and this was followed by a generalized erythematous, macular eruption, with some superimposed pustules. In spite of the fact that patch test elicited a negative reaction, we believe that there is sufficient evidence to consider sulfathiazole to be a contact irritant in this case.

CORNU CUTANEUM

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SAN FRANCISCO

The term cutaneous horn is not exact, as only in appearance does the conditions bearing this name resemble a real horn, and yet this resemblance is often so striking that no better term can be devised.

There are several kinds of cutaneous horns, differing from one another in appearance, in causation and also in histologic structure: the filiform horn; the papillomatous horn, which is a papilloma encased in layers of horny epithelium; the verrucous horn, likewise so encased; a horn arising from the bowl of an open atheroma, and the horn, frequently multiple, arising from a nevus.

THE FILIFORM HORN

The simplest and the most frequently met with is the filiform horn, which resembles a wooden peg slowly growing out from the surface, usually of the face, and results from an error in one of the most interesting functions of the skin.

The epithelial cells are constantly renewed by mitosis of those of the basal layer. As each new cell is born it pushes outward the cells immediately above it and so slowly ascends until finally it is cast off from the surface as an invisible dust.

The epithelial cell is at first a minute soft lump of protoplasm centered by a nucleus, and one of its first functions is to spin out from its body fine threads, the tonofibrils, which crisscross in every direction, binding it firmly to its neighbors and at the same time holding it apart so that there are channels between the cells for the conveyance of nutrient serum and for the elimination of waste products.

As the cell, together with its neighbors, slowly ascends, it gradually loses its vitality, and by the time it reaches the granular layer its life center, its nucleus, has disappeared and is replaced by an oleaginous substance consisting chiefly of cystine, bearing a heavy load of sulfur, admirable as an antiseptic.[1] The dead cell flattens out into a flake con-

1. The large quantity of sulfur is the remarkable feature of cystine, distinguishing it from the other albumins. (Perutz, A.: Die Pharmakologie der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 5, pt. 1, p. 88.) At the upper limit of the mucosa the epidermal cell undergoes a change and three amino acids are formed: tyrosine, tryptophane and cystine, which turn into keratine. (Deseaux, A.; Boutelier, A., and Brocq, P.: Manuel pratique de dermatologie, Paris, Masson & Cie, 1932, p. 23.)

sisting of its own remains and the tonofibrils, all welded together by the oily substance, causing the next layer to look like a clear streak without any individual cells whatever. Presently the oil diminishes and layers of horn appear, still tightly joined by the tonofibrils. Finally this cell, which once was so vitally active, loses the oleaginous substance which had filled its center and infiltrated its walls; its tonofibrils break, loosening it from its neighbors, and it is cast off as an invisible dust. Normally from 6 to 14 Gm. of this dust falls daily from the surface of the skin.[2]

Although the epithelium of the skin is highly individual as regards its cells, it functions as a unit, the cells being born, ascending, making their tonofibrils, dying and turning into horn so evenly that a cushiony, highly resistant, smooth covering for the body is evolved. Under the microscope the epithelium appears to be sharply marked off into layers. This is illusory, as the cells change from an active life to death with a shriveling of their substance and a change into horn slowly and evenly. Interference in the course of this change gives rise to a great variety of symptoms, in the present instance to that of a filiform horn, in which the cells in a limited area, instead of loosening from one another and being cast off as dust, cling closely together and gradually grow out, usually not at all like a horn but as a gray peg, which is often brushed off or may fall spontaneously, only to grow again.

All filiform horns, however, do not resemble wooden pegs. Some of them have wedge-shaped or pointed smooth amber-colored tips, such as the other forms of cutaneous horns generally have. Some dermatologists would limit the term cutaneous horn to lesions having this kind of tip, which is not justifiable. As Riehl has stated, not only these cutaneous horns but also callosities, solid as they may appear, consist not of real horn but of these cornified capsular flakes.[3]

The filiform horn does not consist entirely of epithelial cells. An elongated papilla at its base extends a short distance up through its center, serving to convey the required nourishment. This, however, is far from forming the core of larger horns.

The Type of Skin Facilitating the Occurrence of the Filiform Horn.—The filiform horn may occur on what appears to be normal skin, but it appears more frequently on skin which is dry and flaky, as on the face of an aged person. It also occurs in various conditions in which the horny layer of the skin is thickened and hypertrophied, for instance

2. Pernkopf, E., and Patzelt, V.: Anatomie und Histologie der Haut, in Arzt, L., and Zieler, K.: Die Haut- und Geschlechtskrankheiten, Berlin, Urban & Schwarzenberg, 1933, vol. 1, p. 44.

3. Riehl, G.: Anatomie der Epidermis, in Riecke, E.: Lehrbuch der Haut- und Geschlechtskrankheiten, ed. 3, Jena, Gustav Fischer, 1914, p. 17.

ichthyosis hystrix, the different forms of keratoses of the palms and soles and the hyperkeratoses of gonorrhea or arsenic poisoning; even a mass of callus can become so prominent as to form a horn.[4] A clavus syphiliticus may also at times grow out into a horn.

In my 83 cases the average age of the patients was 51, but the horn may appear in young persons also; one of the patients was a boy of 13. It also can appear anywhere on the skin or semimucosae or even on the mucous membrane. One of my patients had a horn on the hard palate.

Cutaneous Horn and Epithelioma.—The association of a cutaneous horn and epithelioma is the most interesting clinical feature of this condition; the combination is natural, as keratoses, epithelioma and cutaneous horn are all due to erroneous epithelial growth, and all are most often found in the aged. In 12 of my 83 cases the cutaneous horn either occurred coincidentally with epithelioma or had an epitheliomatous base. In some cases it grew out from a keratosis.

Treatment of the Uncomplicated Filiform Horn.—The treatment of the uncomplicated filiform horn is simple. The growth is grasped with a forceps and pulled well out and then ablated with scissors well down into the base. In this way the affected papillae and the mucous layer are removed. As a further guarantee against recurrence, the flat raw surface should be curetted and wiped with trichloroacetic acid. The small wound is treated with boric acid solution and 5 per cent yellow mercuric oxide ointment.

When such a horn springs from a keratosis and any suspicion of epithelioma is present, the curettage and cauterization should be followed by exposure to heavily screened radium or roentgen rays.

CUTANEOUS HORN SPRINGING FROM THE BOWL OF AN OPEN ATHEROMA

This form of cutaneous horn differs in its origin from the filiform. An atheroma is a cyst lined with cutaneous epithelium which is shed into its cavity, usually forming a gruel-like mass. If the top of the cyst is open and the epithelial cells lining the bowl adhere tightly to it and continue to intercohere, they may grow out into a hornlike projection or prong.

In connection with this, Dubreuilh [5] stated that a horn may form in a cyst and finally burst through and project above the surface and that

4. Oppenheim, M.: Die Hypertrophien der Epidermis, in Arzt, L., and Zieler, K.: Die Haut- und filiform Geschlechtskrankheiten, Berlin, Urban & Schwarzenberg, 1935, vol. 2, p. 607.

5. Dubreuilh, W.: Précis de dermatologie, ed. 4, Paris, O. Doin & fils, 1917, p. 425.

most of the horns on the scalp are formed in this way. He further added that an epithelioma developing at the base of such a horn is apt to be particularly malignant.

In my group of cases there was one horn—possibly two—that developed from an atheroma.

CUTANEOUS HORN AS A CORNIFIED PAPILLOMA

The papillary layer of the skin is very thin, about 0.1 mm. ($\frac{1}{250}$ inch) in thickness, but the papillae can grow out to an enormous length. Papillomas 1 inch (2.5 cm.) in length are not so rare, that is to say, papillomas in which the papillae have increased two hundred and fifty times in length. These papillae may become covered with highly cornified epithelium, constituting a horn with a core of fine connective tissue fibers and blood vessels.

An excellent illustration of the structure of a fully developed cutaneous horn of this type was given by Moncorps,[6] from which one may deduce its description. The whole lesion points upward as a spearhead and is composed of layer after layer of horny epithelial cells. These layers loosen and shed off thick dark gray or black shreds. Very interesting is the reduction of the mucous layer down to only one or two cells, which means that these cells cornify much too rapidly and cohere abnormally. The central core is formed by an immensely elongated papilla serving to convey the large capillaries necessary for the nourishment of this comparatively huge structure.

CUTANEOUS HORN DEVELOPING FROM A VERRUCA

A wart is a hypertrophic error in cornification caused by a microorganism, and the mass may plunge down into the skin as a horny nub or the papillae may grow up through the horny mass. When such a wart forms a decided projection, it is called a cutaneous horn, but its treatment, of course, is that of a verruca.

The verrucous and the papillomatous horn afford an interesting contrast. A verrucous horn has its top beset with a number of little prominences corresponding to the tips of the papillae of which it is composed, whereas a papillomatous horn, composed of one immensely elongated papilla, ends in one sharp point or, if it bifurcates—as it sometimes does—in two. Also in contrast is the age of the patient, as warts occur most frequently in childhood or youth.

These distinctions are no trifle, as the verrucous horn has nothing like the sinister meaning attached at times to other forms of cutaneous horn.

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6. Moncorps, C.: Keratosen in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, vol. 8, pt. 2, p. 447.

CORNU CUTANEUM DEVELOPING FROM A NEVUS

The papillae of a nevus may grow out enormously and may form a horn bearing a striking resemblance to those of a ruminant, so much so indeed that in the Middle Ages persons so afflicted or endowed were thought to chew the cud[7] (I say endowed because a person having a good horn often found it a monetary asset).

In my group of cases there was only one example of this, which occurred in a woman 63 years of age. She had a raised brown horny projection with a deeply colored smaller one just anterior to it, and both were situated in a light brown well circumscribed area on the left temple. Horns developing on nevi are apt to be multiple, sometimes remarkably so.

HORN OF THE MUCOSA

The cutaneous horn of the semimucosa is not so rare. I treated one on the red part of the lower lip which developed on a verruca, and many have been reported on the glans penis. In 1 of my cases, mentioned previously, a woman of 66 had a pronged horn on the hard palate. The base was soft, but it cleared off well with the curet and was then cauterized with trichloroacetic acid, with a good result.

BEHAVIOR OF THE BLOOD VESSEL SUPPLY WITH ALL TYPES OF HORN

Consideration of the blood supply is clinically important with all forms of horn. When a horn projecting from an atheroma is curetted out, a glistening white bowl lined with corneous epithelium is exposed. The horn itself is a stout affair built up of layers of corneous epithelium. If epitheliomatous degeneration has taken place, the base of course is soft and fleshy. The filiform horn is also built up of layers of horny epithelium, but it has only the short capillary loop, a papilla projecting up into its base. The horn consisting of an exaggerated verruca has little tendency to grow and seldom reaches a height of 0.5 cm. It has, like a wart, a great number of small papillary projections on its top, or, if the projections cannot be seen because of the overgrowth of epithelium, it may end in a rough rounded nub. A papillomatous horn or one derived from a nevus may be long, slender and well nourished because of having a well developed core of blood vessels and connective tissue.

CONCLUSIONS

What is called a cutaneous horn may be a group of unusually coherent epithelial cells springing out from a circumscribed base or from the bowl of an atheroma, or it may be a highly cornified papilloma or a wart with unusually elongated papillae. A cutaneous horn may also be one of the numerous malformations found in nevi.

7. Moncorps,[6] p. 436. Morgagni, cited by Moncorps.[6]

SULFANILAMIDE AND ALLIED COMPOUNDS

THEIR VALUE AND LIMITATIONS IN DERMATOLOGY

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The discovery of the potentialities of sulfanilamide and its derivatives has been referred to as "the greatest therapeutic achievement in modern medicine." Not since Ehrlich's epoch-making discovery of arsphenamine has a remedy of such specificity and utility been offered to the world. The literature on the clinical and experimental aspects of this group of drugs is enormous. However, several years must elapse before definite indications, proper dosage and methods of administration are determined.

It is our purpose to state our opinion concerning the value and limitations of sulfanilamide and allied compounds in dermatologic practice, including in addition that of dermatologists from all sections of the United States and of many foreign correspondents.[1] Since the literature was reviewed recently by Hughes,[2] we have eliminated many references, citing only a few of those not mentioned by this author.

The history of the development of these drugs and the complete study of their medical and surgical indications, toxic reactions and experimental studies will be found in textbooks, such as that of Mellon, Gross and Cooper [3] and of Long and Bliss.[4]

Several hundred sulfonamide-containing drugs have been synthesized. Our study has been limited to sulfanilamide, azosulfamide, sulfapyridine and the original prontosil.[5] Sulfathiazole, recently introduced, is being

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1. Personal communications to the authors.

2. Hughes, R. P.: The Use of Sulfanilamide in Dermatology, Arch. Dermat. & Syph. **42**:33 (July) 1940.

3. Mellon, R. R.; Gross, P., and Cooper, F. B.: Sulfanilamide Therapy of Bacterial Infections, Springfield, Ill., Charles C. Thomas, Publisher, 1938.

4. Long, P. H., and Bliss, E. A.: The Clinical and Experimental Use of Sulfanilamide, Sulfapyridine and Allied Compounds, New York, The Macmillan Company, 1939.

5. Sulfanilamide is paraaminobenzenesulfonamide. Azosulfamide is disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonate;

(Footnote continued on next page)

tried, with apparently satisfactory results, chiefly in treatment of staphylococcic infections.

TOXIC EFFECTS

Soon after sulfanilamide was used therapeutically it was observed that it caused a large number of unexpected reactions. These included cyanosis, nausea, vomiting, weakness, acidosis, anemia, agranulocytosis, jaundice, splenomegaly, renal insufficiency and optic and peripheral neuritis. In our experience nausea and vomiting were the most common reactions. In hospitalized patients we often have observed unexplained fever. The temperature reaches approximately 102 to 103 F., and the elevation rapidly disappears when administration of the drug is discontinued. Rovira Burzaco 1 noticed that toxic reactions were more common in blonds than in brunets. In our experience toxic manifestations are uncommon in Negroes.

Agranulocytosis is the most serious complication. A complete blood count should be made before treatment with a sulfanilamide compound is started and every few days thereafter. If there is leukopenia, as is often the case in patients with disseminated lupus erythematosus, the drug should be given cautiously. Leukopenia, according to Long and Bliss,[4] should not be considered a contraindication to treatment with sulfanilamide.

The most interesting reactions dermatologically are the eruptions. These are usually morbilliform or scarlatiniform, though purpura, erythema multiforme, varioliform, urticarial, lupus-erythematosus-like, bullous and fixed eruptions and even dermatitis exfoliativa have been observed. The eruptions that we have seen were identical with those resulting from other derivatives of the "coal tar group."

One interesting observation is the photosensitizing property of sulfanilamide. It is generally accepted that during its administration or up to ten days after discontinuance of its use dermatitis may develop in areas exposed to ultraviolet radiation. Patients should be warned against exposure to sunlight. Delayed reaction has also been observed.

We noticed that patients with chancroid and other local infections in which the general health remains good practically never experience serious complications.

Sezary [1] reported a case of contact dermatitis in a worker manufacturing sulfanilamide.

Sensitivity to light following the administration of sulfanilamide is not common and is probably due to a previous disorder of the amino

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this compound has been known as prontosil, as prontosil soluble and as neoprontosil. The original prontosil was the hydrochloride of 4'-sulfamido-2,4-diaminoazo-benzene; this compound is no longer on the market.

acid–porphyrin metabolism. We have exposed patients to ultraviolet radiation after the subsidence of toxic erythemas due to sulfanilamide and have failed to reproduce the eruption, even though the administration of the drug was continued.

LOCAL APPLICATION

Sulfanilamide in powder form has also been used. Dentists have packed sockets after extractions in cases of pyorrhea. Lépinay [6] reported excellent results in the treatment of chancroid by local application of a powder containing 80 per cent sulfanilamide and 20 per cent starch. Fields [1] noticed that uncomplicated chancroids healed in about the same time when sulfanilamide was given by mouth as when it was applied locally.

Others who prefer the local use of sulfanilamide in treatment of chancroid are Sezary,[1] Romero,[1] Covisa,[1] May [1] and Diaz Castro.[1] Gjuric [7] has used sulfanilamide ointment in the treatment of lymphogranuloma venereum.

Balina [1] advised the local use of the dilution of an ampule of azosulfamide in 1,000 cc. of distilled water in wet dressings. It is of value in some dermatoses of streptococcic origin and in subacute eczema. Baccaredda [8] stated that the local application of sulfanilamide was more active than other methods of antisepsis, was always well tolerated and never produced dermatitis medicamentosa. He treated a rather large number of pyogenic infections, with fairly good results. For resistant conditions he advised the simultaneous oral administration of the drug.

We have treated a few patients with impetigo with 10 per cent sulfanilamide in olive oil and hydrous wool fat, and the conditions were cured in four to seven days. Several patients with chancroid treated with local applications of sulfanilamide powder seemed to respond favorably. Experimentally, however, there is little favorable evidence of the value of local therapy. Levaditi has shown that when the drug is injected into the peritoneum of mice and comes in contact with an infectious agent the therapeutic effect is far less than when given by mouth. We have undertaken investigations on the cutaneous absorption of sulf-

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6. Lépinay: Traitement de la chancrelle par la poudre de para-amino-phénylsulfamide ou de ses derivés, Bull. Soc. franç. de dermat. et syph. **45**:1728 (Nov.) 1938.

7. Gjuric, N. J.: Ein neuer Beitrag zur Kenntnis der Klinik und Therapie der Lymphogranuloma inguinale, Arch. f. Dermat. u. Syph. **178**:194, 1938; abstracted, Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1939, p. 394.

8. Baccaredda, A.: Sull'azione dei composti solfamidoazoici e solfamidici in dermatologia, Gior. ital. di dermat. e sif. **79**:429 (April) 1938.

anilamide, but even after the application of a 10 per cent ointment to the skin of the abdomen with friction for half an hour, no traces of the drug could be found in the blood stream.

EFFECT OF SULFANILAMIDE AND ALLIED COMPOUNDS IN VARIOUS DERMATOSES

Lupus Erythematosus.—Since various strains of streptococci are responsible for lupus erythematosus in some cases, it is logical to expect some favorable response to sulfanilamide.

Most of the conditions reported as improved were of the acute or subacute disseminated type. The original prontosil, azosulfamide and sulfanilamide have been used.

In answer to our questionnaire, Sams [1] reported no response in 2 cases of the localized superficial type, in 2 cases of the discoid type and in 1 case of the Libman-Sachs syndrome. Shelmire [1] failed to notice any benefit in 2 cases of acute lupus erythematosus. In 3 cases of this type (probably of the Libman-Sachs syndrome) the patients treated by Becker [1] failed to respond. Wilhelm [1] and Fields [1] found it useless in the treatment of the acute and discoid type. Jaffrey [1] expressed the belief that sulfanilamide has a specific value in selected cases of the acute disseminate type without sensitiveness to light.

Among those who think the drug deserves a trial are MacKee,[1] Peck [1] and Graham.[1] Abramowitz [1] stated the belief that when a patient does not respond to the usual conventional remedies (gold sodium thiosulfate and bismuth compounds) sulfanilamide should be given a trial and that it is particularly useful for the acute type. Grau Triana [1] found considerable improvement in some cases. Saenz reported 3 cases of acute lupus erythematosus in which only temporary improvement was noticed. Wile [1] stated that the drug seemed to be of benefit in 2 cases of the acute type.

Our experience with the discoid type has been unsatisfactory. Fourteen patients were treated with small doses given three times a day for three or four weeks. Administration of the drug to 2 of them was discontinued because of reactions. Of the 12, only 1 showed temporary improvement. All were treated in the outpatient department and were warned against exposure to sunlight. No alteration was noticed in the blood picture. Six patients were given a second course after a week's rest, without improvement.

The discoid type of lupus erythematosus responds poorly to sulfanilamide and allied compounds. The few instances in which success was achieved may be attributed to the sterilizing action of the drug on remote foci of infection. Some patients with the acute disseminated type seem to have been benefited. In consideration of the morbidity of this disease,

empiric treatment seems justified. The wide divergence of opinion regarding the value of these drugs in treatment of the different varieties may be explained on the basis of multiple causation.

Pemphigus.—In answer to our questionnaire, McCauley,[1] Kahn[1] and Ayers and Anderson[1] reported relatively good results with sulfanilamide. McCauley mentioned 3 cases in which the lesions disappeared while the drug was administered. Kahn also reported that the drug was of help to 1 patient, prolonging his life, though he died subsequently of the disease. Ayers and Anderson had favorable results in 3 cases. In 1 the treatment was continued for five weeks; in 1 there was a minor relapse, and in another the lesions improved rapidly within a week. Balina[1] and Laymon[1] noticed improvement in some cases.

On the other hand, Lehmann[1] administered the drug in 2 cases, without benefit. Becker[1] treated 1 patient with pemphigus erythematodes (Senear-Usher) and 1 with pemphigus vegetans, without benefit. Foerster[1] also mentioned failure in 2 cases. Guy and Jacob[1] were unsuccessful in several cases. Wile[1] had tried sulfanilamide extensively in cases of pemphigus and found it of absolutely no value. Peachy[1] reported a case of a boy who failed to respond to sulfanilamide but was benefited by germanin.[9] According to May[1] the lesions may be aggravated.

Sulfanilamide deserves a trial, though the results are not satisfactory according to MacKee,[1] Abramowitz,[1] Saenz[1] and Hopkins.[1] Its use was valueless in the experience of Peck[1] and Romero.[1]

We treated 15 patients with pemphigus with sulfanilamide or sulfapyridine. Various doses were tried. Some patients received 0.6 Gm. (10 grains) three times a day and others as high as 6 Gm. (100 grains) daily. The treatments were continued as long as three to four weeks. Seven patients were women, and 8 were men. Three of them had severe reactions, and administration of the drug to them was discontinued. The duration of the lesions when treatment was instituted varied from three weeks to several months. In 2 patients temporary improvement was noticed, but there was relapse during treatment. In the remaining 10 no improvement was noticed in the lesions of the skin or of the mucous membranes. Five patients died. In no case could a modification of the course of the disease be directly attributed to the drug. The condition remained stationary or became steadily worse. Severe cyanosis was common.

None of the derivatives of sulfanilamide have proved of value in the treatment of pemphigus. A few patients showing temporary allevia-

9. Germanin is reported to be a sodium salt of sym. bis. (*m*-aminobenzoyl-*m*-amino-*p*-methylbenzoyl-*l*-naphthylamino-4,6,8-thiosulfonic acid) urea.

tions had subsequent relapses when administration of the drug was discontinued. A large number of toxic reactions occurred during the treatment. They may be attributed to the low resistance of patients with pemphigus. Unless new derivatives prove more valuable, sulfanilamide will probably be relegated to the group of remedies used empirically in the treatment of pemphigus, to which are credited isolated instances of temporary improvement.

Chancroid.—The treatment of infection with Ducrey's bacillus by means of sulfanilamide having been started in several institutions simultaneously, many authors have claimed priority.

Greenblatt and Sanderson [10] treated 33 patients with 26 to 32 Gm. (400 to 500 grains) of sulfanilamide without resorting to surgical measures other than aspiration of the buboes.

Schwartz and Freeman [11] treated 37 patients, comparing the results in this group with those in 60 patients treated by other methods. The control group required an average of thirty-two days for the lesion to heal and those treated with sulfanilamide fifteen and seven-tenths days. Unruptured buboes yielded rapidly to sulfanilamide therapy. Ulcerations of the glans penis and ruptured buboes were less responsive.

Our correspondents agreed in the value of this treatment. Saunders [1] considered it the treatment of choice. Hopkins [1] and Hughes [1] claimed it to be specific. Saenz [1] and MacKee [1] stated that it deserves a trial. Sainz de Aja [1] reported excellent results in a case of serpiginous chancroid.

The local therapy, preferred by many investigators, has been discussed.

A study of more than 100 patients treated with sulfanilamide, as compared with a control group, was made by Cañizares and Cohen.[12] It was noticed that there was no advantage in giving sulfanilamide to patients with small uncomplicated chancroids. Local therapy with iodoform powder seemed to be sufficient. If the lesions are not controlled promptly, sulfanilamide should be given. Larger lesions are an indication for sulfanilamide, in addition to local therapy. Some phagedenic chancroids respond rapidly; others fail to benefit from the therapy. Excellent results were obtained with ruptured buboes. Rest in bed and aspiration of unruptured buboes are of paramount importance.

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10. Greenblatt, R. B., and Sanderson, E. S.: Sulfanilamide in Chancroid Diseases, Am. J. Syph., Gonor. & Ven. Dis. **23**:605 (Sept.) 1939.

11. Schwartz, W. F., and Freeman, H. E.: Sulfanilamide in the Treatment of Chancroid, J. A. M. A. **114**:946 (March 16) 1940.

12. Cañizares, O., and Cohen, J. A.: Treatment of Chancroid with Sulfanilamide, Arch. Dermat. & Syph. **42**:649 (Oct.) 1940.

Lymphogranuloma Venereum.—The clinical and experimental study of the effect of sulfanilamide in the management of lymphogranuloma venereum was started in different institutions in the early part of 1938.

Some investigators have studied the effect of sulfanilamide in several cases of lymphogranuloma venereum, mostly of the inguinal type. The majority stated that they "obtained excellent results," that the method "is the treatment of choice," that the lesions "showed involution within a month" and that the method "succeeded where other treatment had failed."

Failures also have been reported. According to Greenblatt,[13] sulfanilamide has but a limited place in the treatment of lymphogranuloma venereum. He stated that 50 per cent of the buboes of the disease should subside without therapy.

We have treated more than 200 patients with the inguinal and rectal types of lymphogranuloma venereum during the past four years by various methods of local and internal administration, including intravenous injection of Frei antigen and typhoid vaccine and use of fuadin and antimony and potassium tartrate, alone or combined. During the last two years most of the patients were treated with sulfanilamide. All patients were in bed during the acute stage of the disease, and buboes were aspirated whenever required. Most of them had the inguinal type of the disease. Patients were hospitalized until adenopathy had almost entirely subsided. For purposes of comparison we selected 40 patients with the inguinal type. Of those, 25 were treated with sulfanilamide and 15 with Frei antigen. We found the best results to follow these methods. The average duration of treatment with sulfanilamide was twenty-four days. Under the same conditions the treatment period of the patients treated with Frei antigen (mouse brain antigen administered intravenously every three or four days in increasing doses, starting with 0.1 cc.) was thirty-four days. Relapses were found in 2 cases in each series.

The study of the effect of sulfanilamide in the rectal type of lymphogranuloma venereum is extremely difficult, since it is a chronic process subject to remissions and relapses. We have seen hospitalized patients with this form of the disease improve under various treatments, namely, Frei antigen, intravenous injection of typhoid vaccine and sulfanilamide. Rest in bed and a proper diet seem to be of benefit, since in the clinic good results were not always obtained. In 2 patients with the rectal type who failed to respond to all other therapy the administration of sulfanilamide resulted in decided improvement of the discharge, but the

13. Greenblatt, R. B., in discussion on Greenblatt, R. B.; Dienst, R. B.; Pund, E. R., and Torpin, R.: Experimental and Clinical Granuloma Inguinale, J. A. M. A. **113**:1109 (Sept. 16) 1939.

stricture remained. Sulfanilamide may have some effect on the inflammatory lesions, but when the stricture is of fibrous nature little can be expected of chemotherapy.

In cases of the inguinal type another difficulty arises in the evaluation of therapy. Many patients will be cured spontaneously or with rest in bed and local therapy (aspiration of the buboes and ice bags). These two factors are important in the control of the disease. Conversely, in many cases (about 1 in 20 in our experience) the condition is prone to relapse and has a decided tendency to become chronic. In some instances it persists for as long as two years. These chronic conditions are often resistant to sulfanilamide. The administration of sulfanilamide compared favorably with the injection of Frei antigen intravenously, and small doses caused surprisingly few toxic reactions.

Acne.—The drug is of no value in treatment of acne, according to the majority of authorities. Parkhurst [1] obtained good response in 1 case of the resistant type.

Carbuncle.—Kahn [1] and Lehmann [1] obtained some benefit. Peck [1] stated the belief that the drug deserves a trial in the treatment of carbuncles. Baccaredda [8] observed its failure in 2 cases.

Chronic Streptococcic Dermatitis.—The role of the streptococcus has been emphasized by Sabouraud and Milian and in this country by Mitchell. Baccaredda [8] succeeded in the treatment of various types of dermatitis which he asserted were caused by streptococci.

Sutton and Sutton [1] advised the use of sulfanilamide in cases of "eczema" of the legs, which in their opinion is often due to a remote focus of streptococcic infection. In stopping the spread of acute or subacute infectious eczematoid dermatitis they stated the belief that the drug was of value. Cornbleet [1] stated that chronic exudative dermatitis with edema of the ears is benefited by sulfanilamide.

Chronic Streptococcic Ulcers.—Goodman [14] reported 2 cases of streptococcic ulcer in which the lesion was irresponsive to local therapy but was cured with sulfanilamide in five and three weeks respectively. Sutton [1] and Wilhelm [1] also found the drug of value. Meleney and Harvey [15] emphasized the value of combined use of sulfanilamide and local application of zinc peroxide in the treatment of chronic, undermining burrowing ulcers due to the microaerophilic hemolytic streptococcus.

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14. Goodman, M. H.: Chronic Streptococcic Ulcer of Skin Irresponsive to Local Therapy but Cured with Sulfanilamide, J. A. M. A. **111**:1427 (Oct. 15) 1938.

15. Meleney, F. L., and Harvey, H. D.: The Combined Use of Zinc Peroxide and Sulfanilamide in the Treatment of Chronic, Burrowing, Undermining Ulcers Due to the Micro-Aerophilic Hemolytic Streptococcus, Ann. Surg. **110**:1067 (Dec.) 1939.

Dermatitis Herpetiformis.—The well known tendency of this disease to undergo spontaneous remission makes evaluation of the various methods of treatment difficult. Sainz de Aja [1] obtained good results with sulfanilamide. Dennie [1] and Ayers and Anderson [1] obtained improvement with sulfanilamide. Abramowitz [1] and Fidenza [1] stated the belief that the drug deserves a trial. Saenz found only unsatisfactory response. We tried it in 3 cases, with doubtful results.

Erysipelas and Cellulitis.—The great majority of our correspondents agreed as to the effectiveness of the drug in treatment of erysipelas. Many considered this condition the only specific indication for use of sulfanilamide and its derivatives in cutaneous medicine. In Bellevue Hospital erysipelas has been treated with sulfanilamide compounds since early in 1937. The excellent results in more than 300 cases have been reported by Nelson, Rinzler and Kelsey.[16] The results obtained in cases of cellulitis were also satisfactory.

Templeton,[1] Foerster,[1] Cornbleet,[1] Traub [1] and Lehmann [1] obtained good results in treating cellulitis, the condition following dermatophytosis of the feet in many cases. Kahn [1] obtained no spectacular results with this treatment.

Erysipeloid.—Schoch and Shelmire [17] reported that sulfanilamide in small doses produced prompt resolution in 3 of 4 cases. Michelson [1] and Wilhelm [1] obtained favorable results. Abramowitz [1] thought the drug deserved a trial in this condition. We cured 1 patient in five days.

Erythema Multiforme.—In several instances the duration of the disease was definitely shortened by the administration of the drug. Among those who reported favorable response are Cohen,[1] Burgess,[1] Reynolds [1] and Dennie.[1] Conversely, Simpson [1] found the drug of no value. The bullous type, with severe toxic or septic manifestations, seems more prone to respond.

We treated 8 patients suffering from erythema multiforme with sulfanilamide. No modification of the course of the disease was noticed in 5 patients. In the other 3 its duration was somewhat shortened.

Erythema Nodosum.—The results of the treatment of erythema nodosum with the sulfonamide-containing drugs vary from the poor results obtained by Brunsting [1] to the remarkably good response observed by Reynolds.[1] Simpson [1] reported favorable results with this treatment. F. T. Becker [1] stated that the condition when associated with pharyngeal

16. Nelson, J.; Rinzler, H., and Kelsey, M. P.: Sulfanilamide Treatment of Erysipelas, J. A. M. A. **112**:1044 (March 18) 1939.

17. Schoch, A. G., and Shelmire, B.: Erysipeloid of Rosenbach Successfully Treated with Sulfanilamide, Arch. Dermat. & Syph. **41**:570 (March) 1940.

infections or the presence of remote streptococcic foci elsewhere responded fairly well. We have seen erythema nodosum appear during the administration of sulfathiazole. Evaluation of the therapeutic effect in erythema multiforme and erythema nodosum is greatly hampered because of multiple causation and because of the fact that these diseases are usually self limited.

Furuncles.—Lehman [1] and Cornbleet [1] obtained favorable responses. Brunsting [1] and F. T. Becker [1] found the drug to be of no value. Traub [1] stated the belief that it deserves a trial. Baccaredda [8] failed to obtain improvement with this treatment in 2 cases. We had a few fairly good results, but the drug failed to prevent new lesions.

Granuloma Inguinale.—Sams,[1] Kahn [1] and Greenblatt [1] found no improvement in this disease following the administration of sulfanilamide and its derivatives. Our results have also been unsatisfactory.

Herpes.—For more than a year Shelmire [1] administered sulfanilamide in cases of herpes zoster, with decided benefit. He noticed, however, the same favorable response in cases in which no sulfanilamide was given. He concluded that the eruptions observed during the last few years were caused by an attenuated virus.

Hidradenitis Suppurativa.—Brunsting [1] reported favorable results in cases of secondary undermining of the axillas and groins. Lehmann [1] also was impressed by the effectiveness of chemotherapy in this disease. S. W. Becker [1] noticed some improvement.

Infectious Eczematoid Dermatitis.—Michelson reported favorable results with the drug. We failed to obtain improvement in 2 cases.

Lichen Planus.—Many investigators, including ourselves, found the drug of no value in treatment of this disease.

Lymphangitis.—Saenz [1] expressed the opinion that sulfanilamide is specific for this disease. Foerster,[1] Simpson [1] and Romero [1] found it of value chiefly in the lymphangitis following dermatophytosis of the feet. In several cases of this type we had excellent results.

Lymphedema.—F. T. Becker [1] reported a case of lymphedema of the face associated with infection of the upper respiratory tract in which the condition was resistant to other treatments but was benefited by sulfanilamide. Sezary [1] failed to obtain improvement in a case of elephantiasis of the leg of streptococcic origin.

Pityriasis Rosea.—Fidenza,[1] in the belief that this condition is due to a streptococcus, used sulfanilamide in its treatment, with favorable results. Sainz de Aja [1] stated that the drug deserves a trial in management of this disease. We consider this method unwarranted in treatment of a self-limited dermatosis.

Psoriasis.—Many investigators, including ourselves, have found the drug useless in cases of this disease.

Pustular Bacterid.—We obtained improvement in a case with sulfanilamide.

Pyodermas.—Different types of pyogenic infections have been treated with sulfanilamide and its derivatives. Here, too, opinion is divided. Kahn [1] stated that in 10 cases the lesions healed quicker and with less spreading of the infection. According to Saenz, the treatment is specific for the Tilbury-Fox type of pyoderma. Cornbleet [1] noticed improvement in 1 case of folliculitis. Peck [1] stated the belief that the drug is useless in treatment of pustular dermatoses. Secondary streptococcic infection following dermatophytosis responded well in Dennie's [1] experience. Traub [1] stated that in cases of sycosis vulgaris it deserves a trial. The results obtained by Brunsting [1] were poor. Abramowitz [1] stated that this drug deserves a trial in cases of pyoderma and sycosis vulgaris. Baccaredda [8] successfully treated different types of pyogenic infections.

We agree with those who believe that in treatment of infections which are amenable to cure with local therapy a drug with the potential danger of sulfanilamide should not be given.

Pyoderma Gangraenosum.—Brunsting [1] found the drug of value in a case of pyoderma gangraenosum associated with ulcerative colitis.

Seborrheic Eczema.—Cornbleet [1] and Fields [1] stated that in cases of severe crusted conditions of the scalp the drug is beneficial. Fidenza [1] and Sainz de Aja [1] obtained favorable response in some cases. Again, we believe that sulfanilamide should not be employed for a disease which usually responds well to local therapy.

Syphilis.—Campbell [18] found sulfanilamide and azosulfamide valueless in treatment of rabbit syphilis. In vitro the drugs had no effect on the motility of Spirochaeta pallida. In our cases of mixed venereal infections the administration of sulfanilamide failed to improve the syphilitic lesions.

CONCLUSIONS

Sulfanilamide and allied compounds, though they have revolutionized the treatment of several medical and surgical diseases, are of rather limited value in dermatologic practice. Many dermatoses may respond to one derivative of the group after failure of another.

The inguinal type of lymphogranuloma venereum and, in selected cases, the rectal type respond favorably to these drugs. Their value in treatment of chancroid is unquestionable, but local therapy is still of

18. Campbell, A. D.: Note on the Failure of Sulfanilamide to Affect Syphilis in the Rabbit, Am. J. Syph., Gonor. & Ven. Dis. **21**:524 (Sept.) 1937.

great importance in this disease. In erysipelas, erysipeloid and cellulitis the drugs are of definite value.

For self-limited or easily controlled diseases, such as impetigo, ecthyma or pityriasis rosea, it is inadvisable to use sulfanilamide and its derivatives because of the toxic potentialities.

For diseases such as erythema nodosum, erythema multiforme, dermatitis herpetiformis, pustular bacterids, pyoderma gangraenosum, hidradenitis suppurativa and chronic streptococcic ulcers these drugs deserve a trial when other methods of therapy have failed or when a septic focus of streptococcus is suspected.

For furuncles, carbuncles and sycosis vulgaris in which the staphylococcus is the causative agent the drugs may be of value. New derivatives might prove more active.

For pemphigus and lupus erythematosus the drugs are usually valueless.

The following persons gave their cooperation in this study: E. W. Abramowitz; N. P. Anderson; S. Ayers; P. Balina (Buenos Aires, Argentina); S. W. Becker; L. E. Brunsting; J. F. Burgess; W. B. Cohen; T. Cornbleet; J. S. Covisa (Caracas, Venezuela); C. C. Dennie; J. Diaz Castro; H. A. Dixon; E. L. Eaton; E. P. Fidenza (Rosario, Argentina); R. J. Fields; O. H. Foerster; J. C. Graham; J. Grau Triana (Habana, Cuba); W. H. Guy; N. B. Heller; J. G. Hopkins; F. A. Hughes (Montevideo, Uruguay); F. M. Jacob; W. R. Jaffrey; B. L. Kahn; E. S. Lain; C. W. Laymon; C. F. Lehmann; J. May (Montevideo, Uruguay); G. M. MacKee; F. McCauley; H. E. Michelson; H. D. Parkhurst; C. H. Peachy; S. Peck; H. S. Reynolds; O. Romero (Habana, Cuba); C. Rovira Burzaco (Montevideo, Uruguay); B. Saenz (Habana, Cuba); Sainz de Aja (Madrid, Spain); W. M. Sams; R. L. Saunders; A. Sezary (Paris, France); B. Shelmire; C. A. Simpson; R. Sutton Sr.; R. Sutton Jr.; H. J. Templeton; E. Traub; E. B. Tauber; G. Urena (Mexico, Mexico); F. Weidman; U. J. Wile, and L. F. X. Wilhelm.

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ANDROGEN AND THE XANTHOMATOSES

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Hamblen, Arena and Cuyler [1] studied the output of urinary steroids which they classified as androgen in a case of Hand-Schüller-Christian disease. They found values ten times as large as the normal ones and felt that this increase was related to the general disturbance of lipoid metabolism rather than to an excessive activity of the gonads or of the adrenal cortex. Their patient, a male infant, did not excrete any sodium pregnandiol glucuronidate, a metabolite of secretion from the corpus luteum. After reading this report, we decided to assay the urine of a number of subjects with diseases of the skin classed as lipoidoses. This decision was based on the hypothesis that a relation exists between Hand-Schüller-Christian disease and at least some of the lipoidoses. This, however, is still a debatable subject, although cases of mixed varieties and transition states between have been reported and presented before various dermatologic groups.

METHOD OF STUDY

Subjects with various types of diseases of the skin, such as cutaneous xanthomatoses, were selected. Twenty-four hour urinary samples were extracted by a method which is a modification of that described by Dingemanse.[2]

The specimen of urine was acidified with 150 cc. of concentrated hydrochloric acid. The mixture was extracted with three separate samples of carbon tetrachloride (125 cc. each), a reflux condenser being used for two hours each time. The carbon tetrachloride fractions were united and evaporated to dryness under reduced pressure, and the residue was taken up in 100 cc. of ether. The ether was extracted in a separatory funnel three times with a saturated sodium bicarbonate aqueous solution and five times with 10 per cent sodium hydroxide. The

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1. Hamblen, E. C.; Arena, J. M., and Cuyler, W. K.: Hand-Schüller-Christian Disease: Report of Case in Which Urinary Androgens Were Titrated, Am. J. Dis. Child. **60**:352 (Aug.) 1940.

2. Dingemanse, E.; Borchardt, H., and Laqueur, E.: Capon Comb Growth-Promoting Substances ("Male Hormones") in Human Urine of Males and Females of Varying Ages, Biochem. J. **31**:500 (April) 1937.

ether was then washed with 10 per cent sulfuric acid and three times with distilled water. An aliquot part of the ether solution was decolorized with activated charcoal and evaporated to dryness under reduced pressure. The residue was taken up in 10 cc. of 60 per cent ethyl alcohol. Two cubic centimeters of a solution of metadinitrobenzene (2 Gm. in 100 cc. of 95 per cent alcohol) and 2 cc. of a 15 per cent aqueous solution of potassium hydroxide were added. Colorimetric estimation was made after ninety minutes with a spectrophotometer (technic of Neustadt [3]).

A sample of crystalline androsterone was dissolved in 60 per cent alcohol and treated with metadinitrobenzene and potassium hydroxide as previously described and used as a control. A blank solution was prepared by adding activated charcoal to ether and treated as described.

Relation of Excretion of 17-Keto Steroids to That of Total Cholesterol in Patients with Lipoidoses*

Patient	Disease	17-Keto Steroids, Mg. per 100 Cc. Blood	Total Cholesterol, Mg. per 100 Cc. Blood
L. P.	Xanthoma tuberosum and diabetes	17	410
P. G.	Xanthelasma	6	224
C. N.	Xanthoma tuberosum	19.3	363
J. N.	Necrobiosis lipoidica	19.5	195
M. K.	Xanthoma tuberosum	19.5	878
K. B.	Xanthoma disseminatum	6.0	205
E. G.	Necrobiosis lipoidica	8.0	157

* 17-keto steroids are a group of compounds which include the androgens. Some of them have biologic activity similar to the testis secretion, while others are inert. They originate in the gonads, in the adrenal cortex and possibly from other sources.

COMMENT

All investigators agree that at present the colorimetric procedure measures 17-keto steroids and not the true androgen. The term androgen usually refers to the comb growth–stimulating material, which is present in the urine in a lower concentration than that of 17-keto steroids. Assays were not made of the comb growth–stimulating material in our patients' urines, since the 17-keto steroids were within the normal range. Our method of assay differs from that of Hamblen and his co-workers only in minor details, and in our opinion their values should properly be called 17-keto steroids and not androgen. In their report and the photographs submitted, we have been unable to find evidence of increased production of androgen. In the cases of disturbance of lipoid metabolism we have studied, we have failed to find an elevation in the 17-keto steroids similar to that reported by Hamblen, Arena and Cuyler. We are unable to give any explanation for this discrepancy in results other than that the kinds of metabolic disturbance in the patients we studied

3. Neustadt, R.: Photo-Colorimetric Method for Determination of Androsterones in Urine, Endocrinology **23**:711 (Dec.) 1938.

are different in some essential from those in patients with Hand-Schüller-Christian disease. Are findings, such as those reported by Hamblen, Arena and Cuyler, of increased steroids a regular occurrence in Hand-Schüller-Disease? It appears from our results that an increase of the 17-keto steroids is not characteristic of the cutaneous xanthomatoses. The question arises then whether Hand-Schüller-Christian disease and the xanthomatoses familiar to the dermatologist belong to the same group of metabolic disease.

SUMMARY

A report is cited from the literature in which an increased quantity of androgen is stated to have been found in the urine of an infant with Hand-Schüller-Christian disease. Reasons are given for our belief that the material assayed was probably not androgen but should have been more properly labeled 17-keto steroids.

The urine of 7 subjects with varieties of lipoidoses contained normal quantities of 17-keto steroids. Androgen was not increased in amount. Our patients did not show clinical evidence such as is commonly present with increased quantities of androgen.

Since the results reported by Hamblen, Arena and Cuyler for Hand-Schüller-Christian disease and ours for the cutaneous xanthomatoses differ, the question arises whether the former disease belongs metabolically to the group of diseases which includes lipoidoses of the skin.

GASTROSCOPIC OBSERVATIONS IN ROSACEA

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Subsequent to the observation of Ryle and Barber [1] of hypoacidity or anacidity in many patients with rosacea, numerous investigators have reported conflicting results. The latest complete series of analyses by Smith and McLachlan [2] and by Reyn [3] with adequate controls revealed that changes in gastric acidity were equally common in other dermatoses. They further stated that their observations did not detract from the well established fact that strict dietary treatment in combination with large doses of hydrochloric acid brought about great improvement in the rosacea.

In view of the dietary indiscretions indulged in by the majority of patients with rosacea and the usual history of gastric disturbance, it is likely that some degree of gastritis is nearly always present. In the belief that this is so, a new method of approach has been adopted: direct visualization of the gastric mucosa. By means of the gastroscope, the gastric mucosa has been visualized in patients with rosacea and in a suitable series of controls.

Gastroscopic examination [4] revealed various pathologic changes in the gastric mucosa. In cases in which there were flattening and thinning of the mucosa with loss of fold formation and increased visibility of the submucosal blood vessels, atrophic gastritis was diagnosed. In cases in which there were increased rigidity of the folds, which would not flatten out or would flatten only with considerable distress to the patient, edema of the mucosa and semiverrucous projections and, at times, minute erosions, a diagnosis of hypertrophic gastritis was made. When the changes were confined more to the surface and less to the parenchyma, superficial gastritis was diagnosed. These changes consisted in pronounced superficial reddening, varying degrees of superficial edema and sometimes shallow ulcers.

Read before the Montreal Dermatological Society, Nov. 9, 1940.

From the Department of Dermatology, the Montreal General Hospital.

1. Ryle, J. A., and Barber, N. W.: Gastric Analysis in Acne Rosacea, Lancet **2**:1195 (Dec. 11) 1920.

2. Smith, M. S., and McLachlan, A. D.: Gastric Analysis in Diseases of Skin, Especially in Rosacea, Brit. J. Dermat. **47**:181 (May) 1935.

3. Reyn, A., abstracted, Wise, F., and Sulzberger, M. B.: Year Book of Dermatology, Chicago, The Year Book Publishers, Inc., 1936, p. 499.

4. Dr. J. J. Day, of the department of medicine, the Montreal General Hospital, carried out these examinations.

Two groups of patients were studied, one composed of persons suffering from rosacea of varying degrees of severity and the other of persons with unrelated dermatoses. In both groups no patient was included with a condition that was associated with any underlying disturbance that would in itself produce a gastritis. A preliminary analysis of gastric contents was performed for all patients studied. The test meal consisted of 150 cc. of 5 per cent alcohol taken in the fasting state. Specimens of gastric secretion were examined at intervals of twenty

TABLE 1.—*Gastroscopic Examination of Patients with Rosacea*

Patient	Age	Duration of Disease, Years	Digestive Symptoms	Gastric Analysis	Gastroscopic Examination
Mrs. F.	37	8	.....	Achlorhydria*	March 1939: Hypertrophic gastritis November 1939: Improved from previous examination
Mrs. R.	36	14	+++	Normal	Superficial gastritis
Mrs. D.	42	7	++	Unknown	Early atrophic gastritis
Mrs. C.	43	Years	+++	Hyperchlorhydria	April 1939: Superficial and atrophic gastritis November 1939: Mucosa good color; suggestion of fold formation
Mrs. N.	37	Years	+++	Normal	Superficial and atrophic gastritis
Mr. D.	38	Years	+++	Hyperchlorhydria	Severe hypertrophic gastritis; duodenal ulcer
Mr. T.	50	7	—	Achlorhydria	Slight superficial gastritis
Mrs. R.	34	15	+	Normal*	Slight superficial gastritis
Mr. N.	28	1	+	Normal	Slight superficial gastritis
Mrs. B.	31	3	—	Normal	Normal
Mrs. B.	40	12	—	Hypochlorhydria	Early atrophic gastritis
Mrs. W.	26	3	0	Normal*	Early atrophic gastritis
Mrs. H.	40	Years	+++	Hypochlorhydria	Mild hypertrophic gastritis
Mr. B.	60	..	—	Normal	Superficial gastritis
Mr. A.	40	..	—	Normal	Superficial gastritis
Mr. A.	68	Years	—	Normal	Superficial gastritis
Mrs. L.	35	4	+++	Achlorhydria	Atrophic gastritis
Mrs. P.	17	1	0	Hypochlorhydria	Superficial gastritis; suggestions of possibility of atrophic gastritis later; acne vulgaris
Mr. F.	62	Years	0	Normal	Atrophic gastritis

* With histamine.

minutes. When indicated, 0.5 mg. of histamine phosphate was given orally. Hydrochloric acid readings of 20 to 40 were considered to be within the normal range.

Gastroscopic examination was also performed in the fasting state. There was, however, preliminary medication one hour before with phenobarbital, 3 grains (0.2 Gm.), and atropine, $\frac{1}{150}$ grain (0.043 mg.), by mouth.

The results of the studies may be noted in tables 1, 2 and 3.

Of the 19 patients with rosacea 6 (33 per cent) had achlorhydria or hypochlorhydria; 2 (11 per cent), hyperchlorhydria, and 10 (56 per

cent), normal secretion; for 1 patient the result was not known. In the control cases, the figures were 7 (47 per cent) with a low secretion, 6 (40 per cent) with a normal amount and 2 (13 per cent) with an increased amount.

TABLE 2.—*Gastroscopic Examination of Control Patients with Various Dermatoses*

Patient	Age	Duration of Disease, Years	Digestive Symptoms	Gastric Analysis	Gastroscopic Examination	Diagnosis
Miss B.	25	10	..	Achlorhydria	Chronic hypertrophic gastritis	Atopic eczema
Mrs. R.	46	Years	+++	Achlorhydria*	Atrophic and hypertrophic gastritis	Prurigo and possible pernicious anemia
Mr. A.	32	2 mo.	..	Hypochlorhydria*	Normal	Alopecia areata
Mr. M.	50	1	..	Hyperchlorhydria	Normal	Chronic urticaria
Mr. H.	23	10	..	Normal	Normal	Atopic eczema
Miss S.	24	15	..	Hypochlorhydria	Superficial gastritis	Diffuse alopecia areata
Mr. F.	54	Years	..	Normal	Normal	Lupus erythematosus
Mr. C.	..	..	..	Hypochlorhydria*	Normal	Lichen planus hypertrophicans
Mrs. T.	30	1	..	Hypochlorhydria*	Normal	Dermatitis venenata of the face
Mr. P.	67	2	..	Hypochlorhydria	Normal	Lupus erythematosus
Mr. S.	66	Months	..	Normal	Superficial gastritis	Chronic urticaria
Mr. I.	50	1	..	Hyperchlorhydria	Normal	Generalized eczema
Mr. C.	44	4	..	Normal*	Normal	Lupus erythematosus
Mr. C.	46	Months	..	Normal	Normal	Extensive eczema
Mr. C.	50	10	..	Normal	Normal	Generalized eczema

* With histamine.

TABLE 3.—*Comparison of Results of Examination of Patients with Rosea and of Control Patients with Unrelated Dermatoses*

	Patients with Rosacea		Control Patients	
Sex				
Male	7		11	
Female	12		4	
Age	26-68		23-67	
Gastrointestinal symptoms	9/10		1/10	
	Number	Per Cent	Number	Per Cent
Analysis of gastric contents				
Hyperacidity	2	11	2	13
Normal	10	56	6	40
Hypoacidity	6	33	7	47
Results of gastroscopic examination				
Normal	1	5	11	73
Superficial gastritis	8	42	2	13
Atrophic gastritis	5	26	0	0
Hypertrophic gastritis	3	16	1	7
Mixed	2	11	1	7

Of the 9 of the control patients picked at random and studied medically, only 1 had gastrointestinal complaints; this patient had a

mixed type of gastritis with histamine achlorhydria. Of 10 patients with rosacea studied medically, only 1 had no gastrointestinal complaints; this patient, a woman, had an early atrophic gastritis with a normal acid curve.

The results of gastroscopic examination were interesting. Of the patients with rosacea, the gastric mucosa was normal in only 1 and showed superficial gastritis in 8, atrophic gastritis in 5, hypertrophic gastritis in 3 and mixed atrophic and superficial gastritis in 2. In the control group, examination of the gastric mucosa revealed no pathologic changes in 11 patients, superficial gastritis in 2, hypertrophic gastritis in 1 and mixed atrophic and hypertrophic gastritis in 1.

COMMENT

It is known, according to Hurst,[5] that foci of infection, emotional disturbances, endocrine disorders and dietary indiscretions may be responsible for the production of gastritis. It is also well established that one or more of these factors may be present in patients with rosacea. What is then the relation between the gastritis and the rosacea? Are they both directly dependent on the underlying factor or factors and unrelated directly to each other? Or is the gastritis the precursor and the cause of the rosacea? The improvement in the gastritis and in the rosacea sometimes seen after the eradication of the underlying disorders stresses the importance of the latter theory. Yet the improvement in the disease as a result of the treatment of the gastritis by the administration of hydrochloric acid or of alkali, with a proper dietary regimen, seems to bear out the importance of the gastritis as a direct etiologic factor in rosacea. Certainly the objective improvement in the gastritis noted in 2 of my patients on repeated gastroscopic examination with coincidental improvement in the rosacea as a result of treatment of the former is evidence in favor of this theory. This phase of the subject needs further study.

SUMMARY

1. Nineteen patients with rosacea and 15 with varying dermatoses as controls were studied.

2. The incidence of hypochlorhydria and achlorhydria in patients with rosacea was not greater than with other dermatoses.

3. The gastric hydrochloric content was not dependent on the duration or on the degree of severity of the rosacea.

5. Hurst, A. F.: Clinical Importance of Achlorhydria, Brit. M. J. **2**:665 (Oct. 13) 1934.

4. Gastritis of varying degrees of severity was present in all except 1 of the patients with rosacea, whereas with the control dermatoses only 4 patients showed evidence of gastritis.

5. As a rule, severe changes in the gastric mucosa were associated with abnormality in the hydrochloric secretion.

6. Achlorhydria was always found to be associated with long-standing gastritis.

7. Repeated gastroscopic visualization in 2 treated patients showed coincidental improvement of both the gastritis and the rosacea.

Dr. J. F. Burgess, chief of the department of dermatology, granted permission to publish this material.

Clinical Notes

SENSITIVITY OF THE SKIN TO FLUORESCENT LIGHT

ARTHUR P. R. JAMES, M.D., TOLEDO, OHIO

A new type of illumination produced by daylight fluorescent mazda lamps is coming into wide use, particularly in industry. In the development of a new source of light for general purposes, engineers are always concerned with confining the radiant energy emitted by the lamp within the wavelength range of natural sunlight. The glass tubing of the fluorescent lamp has a composition which absorbs all the energy of the shorter wavelengths than the short wave limit of sunlight. Nevertheless, dermatologists must be alert to the possibility of sensitivity to this type of lighting. I am reporting 2 cases to illustrate this fact.

REPORT OF CASES

CASE 1.—A white woman aged 21, an employee of an electrical company, complained of a dermatitis of three weeks' duration involving her face, most evident on the eyelids. Her history from a dermatologic standpoint was normal. Routine patch tests gave negative results. The use of all cosmetics was forbidden. She was instructed to cleanse her face with a solution of corn starch in milk. One quarter skin unit of roentgen rays (75 r) was given at weekly intervals. Calamine lotion with 1 per cent phenol and 1 per cent menthol was prescribed. Her condition became progressively worse, and she stopped work. She improved rapidly at home, returned to work and immediately had a recurrence of the dermatitis. Obviously the causative factor of the condition was encountered at work. On checking her history with this new information I learned that a fluorescent lamp had been installed at her desk three weeks prior to the start of the cutaneous condition. A single 40 watt daylight fluorescent tube was mounted 3 feet (90 cm.) above her desk, producing a level of illumination at her desk of 22 foot-candles. She was instructed to work with the lamp turned off, and within two weeks her skin was normal. After her skin had remained normal for three weeks, she cooperated by working in the light again for a half day and experienced a severe recurrence of her dermatitis. This girl was a brunette with a definite history that she could tolerate more sunlight than the average person. At the time of writing her skin is normal.

CASE 2.—A white woman aged 27, an employee of a glass-manufacturing company, referred by Dr. Kenneth R. Howard, presented a dermatitis involving her face and the back of her neck. The condition was most severe on the eyelids. She stated that fluorescent lamps had been installed in her office just prior to the start of the eruption. In this case four 40 watt daylight fluorescent tubes were installed 9½ feet (290 cm.) above the floor, and the patient worked with her back to the last unit at a distance of 8 feet (240 cm.). Foot-candles measured on the patient's desk were horizontal 5, vertical 4 and in direct line 8. Her employer moved her office. However, she was still exposed to this radiation for ten to thirty minutes each day when she returned to her old office to consult her files. Routine patch

tests, including tests made with all cosmetics, gave negative results, and she received the same local therapy as that administered in case 1. She improved slowly. She stated that her skin itched and burned for hours after every exposure to the fluorescent light. She was instructed to apply a tannic acid solution several times daily to the affected parts and to wear colored polaroid glasses. Under this regimen her skin showed rapid improvement. Whenever she did not apply the tannic acid solution or failed to wear her glasses, exposure to the fluorescent light was followed by dermatitis. This patient was a blonde with a fine skin. She stated that she was careful to avoid sunlight in summer because her skin would not tolerate it. Unlike patient 1, patient 2 is the type one might expect to become sensitized to light of different wavelengths. At the time of writing her skin is normal.

COMMENT

Since this type of lighting is so desirable from a general standpoint, it is rapidly becoming popular, and undoubted'y many cases of sensitivity will be encountered. The fact that the wavelengths of the radiant energy of this type of lighting are confined to the range of natural sunlight would influence the belief that a person who would tolerate sunlight would tolerate this light. Case 1 disproves this belief. A person may show sensitivity to an isolated band of light yet tolerate it when it is mixed with light of other wavelengths.

With this fact in mind a new tube has been produced, termed "soft white," which will give off added red rays. It is hoped that the addition of the red rays will neutralize the effect of the rays producing the dermatitis. Progress in this regard will be reported in a later paper. In the meantime temporary protection may be afforded the sensitized person by the use of a tannic acid solution and the wearing of polaroid glasses at the time of exposure.

SULFANILAMIDE IN GLYCERIN IN THE LOCAL TREATMENT FOR PYODERMAS

EVERETT S. LAIN, M.D., OKLAHOMA CITY

Medical literature is now replete with reports of the administration of sulfanilamide and its derivatives in various diseases, largely those in which cocci or allied organisms have been proved a causative factor. Hughes[1] has recently published an excellent bibliography and a brief review of the treatment of multiple dermatologic conditions with sulfanilamide. His review, however, reveals that the use of this marvelous drug, with but few exceptions, has been limited to its administration by mouth, hypodermically or intravenously. The exceptions are its use by certain physicians as a dusting powder on open infected wounds or ulcers.

After reviewing Hughes's citations and those of others, I have failed to find that sulfanilamide has been applied locally in solution, doubtless for the reason that according to manufacturing chemists sulfanilamide is soluble only to approximately 0.8 per cent in water, although it is much more soluble in alcohol or glycerin.

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1. Hughes, R. P.: The Use of Sulfanilamide in Dermatology, Arch. Dermat. & Syph. **42**:33 (July) 1940.

It occurred to me nearly twelve months ago that the administration of this drug internally, with its attendant nausea, headaches, anorexia and occasional cutaneous reactions, might be avoided in the treatment of nonfebrile and obviously localized infections if an absorbable solution was used. Therefore, I had prepared a supersaturated solution of powdered sulfanilamide in glycerin for local application, which has proved so successful and gratifying that it has now come to be used in routine treatment in the state university clinic and in the private practice of my associates and myself in all cases of impetigo, acute infectious dermatitis of the ears, scalp or feet, coccigenic sycosis, folliculitis, septic ulcers and other streptococcic and staphylococcic infections.

The solution is easily made in the physician's office by the addition of 1 to 2 drachms (4 to 8 Gm.) of powdered sulfanilamide to each ounce (30 cc.) of slightly warm (not hot) glycerin. If more powder than the glycerin will dissolve is added (though not to the degree of a stiff paste), the adherent unabsorbed powder serves as an excellent protective dressing. Application of the solution may be made with a cotton swab or with the fingers directly to the affected areas two or three times daily without bandaging, although the time required for a cure is much shortened if daily applications are made with thin strips of gauze saturated with this solution and bandaged. If sheets of paraffin paper are applied over the saturated gauze under the bandage, the diseased parts will be kept moist and comfortable and the crusts, which usually adhere to the gauze, will come away with the change of the first dressing. There may occur a mild smarting at the first application due to the action of the glycerin on the raw areas, but this disappears after a few seconds, and the dressing then becomes soothing and comfortable.

The favorable action of sulfanilamide in the treatment of certain pyodermic processes when administered internally has already been sufficiently emphasized by others. It has been almost forgotten, however, that glycerin is mildly germicidal, strongly depleting and one of the most reliable antiphlogistic agents. I have not thus far observed a single case of sensitivity to this dressing.

I have also tried the incorporation of sulfanilamide in various ones of the oily and of the newer water-soluble ointment bases, but none of these preparations has given such rapid and satisfactory results as the solution of sulfanilamide in glycerin. More recent experiments may prove that other members of the sulfanilamide group are of equal value, though not so economical.

Medical Arts Building.

PITYRIASIS ROSEA WITH VESICULAR LESIONS ON THE PALMS

W. F. Spiller, M.D., and E. B. Ritchie, M.D., Galveston, Texas

The following record is that of a patient recently seen in the outpatient clinic of the John Sealy Hospital.

REPORT OF A CASE

G. S., a woman physician aged 30, seen first on Jan. 2, 1941, presented a papulosquamous eruption of one day's duration on the trunk and extremities.

From the Department of Dermatology and Syphilology, University of Texas Faculty of Medicine.

It was typical of pityriasis rosea. The "herald plaque," of ten days' duration, was present on the left breast. The eruption extended below the elbows to the wrist, and both palms showed numerous sago-like vesicles. There were no vesicles on the soles. The patient stated that the vesicular lesions on the palms appeared two days before the eruption on the body. Examination of the tops of the vesicles showed no mycelia or Acarus scabiei. The Wassermann reaction of the blood was negative, and the blood count showed nothing of significance. The eruption cleared in three weeks after treatment with ultraviolet radiation and calamine lotion.

COMMENT

Lesions of the palms in cases of pityriasis rosea are rare, and vesicular lesions of the palms have been only infrequently reported. The case herein described was thought to be of sufficient interest to warrant this brief report.

AN INSTRUMENTAL AID IN THE TREATMENT OF TELANGIECTASES

JACQUES P. GUEQUIERRE, M.D., PHILADELPHIA

While applying pressure to a giant spider nevus prior to treatment, I realized that if the glass slide had some perforations I could easily obliterate the "feeder" vessels which stood out so prominently. It was also apparent that if the perforations were irregularly distributed different vessels could be treated at the same time merely by shifting the slide without lifting it.

Two slides were made,[1] one corresponding to the ordinary laboratory glass slide and the other to a short glass stirring rod with one end flattened and containing a single perforation. The latter was most useful in treating telangiectases on the nose and about the angle of the eye. Successful results were obtained by using electrodesiccation or electrocoagulation. For the larger veins on the nose, obliteration was more rapid when multiple punctures were made along the length of the vessels. The pressure of the slide eliminated bleeding and greatly facilitated treatment.

The cost of these slides was high owing to breakage in drilling perforations. They were, moreover, easily broken in the office. It was thus apparent that a noninflammable transparent plastic material was desirable.

In plexiglas[2] I found the desired plastic material. It has a colorless transparency and is hard, elastic and chemically stable. It may be bent or formed into various shapes without developing strains or blemishes and is practically nonbreakable. Its cost is one-fifth that of ordinary glass. Plexiglas does not ignite readily but burns slowly after having been warmed and ignited by a flame.

1. The slides were made by the Catalin Work Shop, 112 South Twentieth Street, Philadelphia.

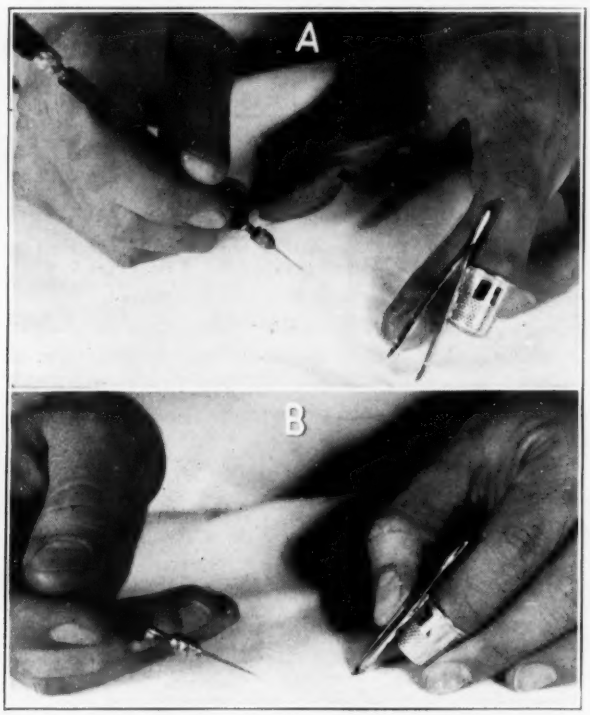
2. Plexiglas is made by the Robin & Hass Co., Philadelphia, and by E. I. du Pont de Nemours & Co., Inc., Wilmington, Del.

The electric spark, used in the perforation or played directly on the slide,[1] does not ignite the material.

A "THIMBLE FORCEPS" FOR EPILATION

JOSEPH M. SHELTON, M.D., WASHINGTON, PA.

The picking up and laying down of the epilating forceps during the process of electrolysis has always been a time-wasting procedure. This can easily be obviated by attaching one side of the forceps to an ordinary metal sewing thimble,



Use of "thimble forceps," showing the position of the hands *(A)* during insertion of needle, with forceps not in use, and *(B)* during process of removing hair.

as shown in the photograph. A metal glue, such as "metallic-X," can be used satisfactorily provided that the instrument is not to be sterilized by heat.

With the thimble on the left forefinger the forceps can be maintained in the proper position. This will allow the thumb and other fingers to be used for stretching the skin prior to the insertion of the electrolysis needle (fig., *A*). On withdrawal of the needle, the forceps is ready to be compressed between the thumb and the forefinger (fig., *B*).

Washington Trust Building.

From the Pittsburgh Skin and Cancer Foundation, Pittsburgh.

News and Comment

HISTOLOGIC SECTIONS ON CERTAIN NEVI AND CUTANEOUS CANCER NOW PURCHASABLE

In the March 1941 issue of the ARCHIVES it was stated that fifteen sets of thirty-five histologic sections each could be purchased, covering various types of nevi, precancerous dermatoses and cancer. These sets were used in the special course on histopathology at the annual meeting of the American Academy of Dermatology and Syphilology in Chicago, Dec. 8 to 11, 1940.

Since that time most of the sets have been sold, preference having been given to teaching institutions and to persons engaged in teaching. By this time such institutions and persons have had time to send in their orders, and accordingly the remainder of the sets will be sold to other persons on receipt of applications. The charge per set and syllabus is $25, payable to Registry Account, Army Medical Museum. The address is Curator, Army Medical Museum, War Department, Washington, D. C.

THE AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

A written examination will be given by the American Board of Dermatology and Syphilology on Nov. 3, 1941, and an oral examination, on December 12 and 13. Applications for the former should be in the hands of the Secretary, Dr. C. Guy Lane, 416 Marlborough Street, Boston, by September 23, and for the latter, by November 8.

DEATHS

Dr. Elmore B. Tauber of Cincinnati, Ohio, died on June 24, 1941.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

HISTAMINASE IN THE TREATMENT OF COLD ALLERGY. T. W. BAKER, J. A. M. A. **114**:1059 (March 23) 1940.

Baker studied 2 patients with cold allergy as evidenced by the development of redness, edema and urticarial wheals on the exposed skin. Acceleration in the pulse rate, a drop in the blood pressure and the development of headache were noted shortly after a test immersion of a hand in water at 10 C. (50 F.) for ten minutes. Successful results were obtained by Baker in the 2 patients with a combination treatment of (1) graded desensitization to cold and (2) administration of histaminase by mouth in a total dose of 515 and 300 detoxifying units respectively. A relapse in 1 patient responded favorably to 100 units of histaminase alone.

PARAFFINOMA SIMULATING SEQUELAE OF VENOUS STASIS: A MALINGERER'S DEVICE. W. W. HEYERDALE and J. W. MADER, J. A. M. A. **114**:1066 (March 23) 1940.

The patient received an injection of hot wax into the subcutaneous tissues of the left ankle twenty-five years before he was examined by Heyerdale and Mader. The resultant swelling was sufficient to allow him to avoid military service. The brown induration present when he was examined simulated the late results sometimes seen around varicose veins which have been untreated.

A CASE OF COLD URTICARIA WITH AN UNUSUAL FAMILY HISTORY. R. L. KILE and H. A. RUSK, J. A. M. A. **114**:1067 (March 23) 1940.

A married woman of 25 complained of the development of urticaria after exposure to cold. A chill and fever lasting for from four to six hours also occurred. Often stiffness of the joints and erythema in the adjacent tissues were noted. Kile and Rusk were able to obtain records of 23 instances of cold urticaria in a total of 47 relatives known to the patient or to her father. Thirteen of the 23 involved relatives were females. The father of the patient also had hay fever, but there were no instances of other types of allergy. The level of the blood potassium was found to be elevated. Treatment by means of attempted desensitization was unsuccessful, as also were the administration of large doses of splenic extract and histaminase and a dietary regimen low in sodium and high in potassium, with 20 grains (1.3 Gm.) of potassium chloride three times a day and crystalline insulin twice a day for one week.

SYPHILIS CASE FINDING IN INDUSTRY. A. E. RUSSELL, J. A. M. A. **114**:1321 (April 6) 1940.

Russell points out that there are over 15,000,000 persons in the mining, metal and manufacturing trades in the United States. He makes a plea for a concerted effort in the industries by the workers, the health officers and the practicing physicians to find and treat all persons with both infectious and noninfectious syphilis. Routine Wassermann tests of the blood should be performed on all new applicants and at each physical reexamination. Patients with syphilis should not be discharged if they continue treatment. Educational programs should be devised to teach the employees the facts about venereal diseases.

ANGIONEUROTIC EDEMA DUE TO TOBACCO SENSITIVITY AND THROMBOANGIITIS OBLITERANS IN THE SAME PATIENT. S. SILBERT, J. A. M. A. **114**:1442 (April 13) 1940.

A patient aged 44 had suffered from angioneurotic edema for eight years. He had also had several attacks of phlebitis during a period of five years, with the onset of symptoms and signs revealing a definite thromboangiitis obliterans. The patient's skin on testing was found to be hypersensitive to tobacco. He stopped smoking, and Silbert attributed the favorable response which occurred in both conditions to this alone. Silbert draws attention to the rarity of two shock centers and also to this case being the first instance reported of angioneurotic edema due to tobacco.

RAT MITE DERMATITIS. L. F. WEBER, J. A. M. A. **114**:1442 (April 13) 1940.

Weber reports a series of 5 patients from a department store in Chicago who had wheals and papules, many with a central punctum. The lesions cleared if the patients stayed away from work, but they noticed recurrences when they had business in the basement of the store. It was discovered that many rats had been destroyed just prior to the beginning of the trouble. The rat mites were then attracted to the human hosts and were discovered by Weber on the patient's skin, on dead rats and on boxes of merchandise. Hydrocyanic acid gas destroyed the mites.

INDUSTRIAL DERMATITIS FROM GLOVES: EFFECT OF DERMATOPHYTOSIS (RINGWORM); "GLOVE PHYTIDS." W. D. NORWOOD and E. E. EVANS, J. A. M. A. **114**:1523 (April 20) 1940.

Norwood and Evans found that 84 per cent of the employees examined in a large industrial plant showed clinical evidence of dermatophytosis of the toes. More time was lost in a year because of dermatophytosis than for all other cutaneous diseases combined, infection excepted. They studied 20 men who had eczematous rashes on the hands. The workmen wore leather gloves for protection and the eruption usually improved when gloves were not worn. However, permanent cure was not obtained until the focus of dermatophytosis on the feet was eradicated. It was thus concluded that the factors involved in the causation of the eczematous eruptions of the hands included both the fungous focus on the feet and the maceration following the wearing of the leather gloves. It was further noted in support of this supposition that eczema of the hands was fifteen times as frequent in workers who wore leather gloves as in those who did not.

HEMANGIOMAS OF THE SKIN. G. E. WARD and E. E. COVINGTON, J. A. M. A. **114**:2069 (May 25) 1940.

Basing their conclusions on their experience in treating 127 hemangiomas present in 94 patients, Ward and Covington consider that radium is usually the treatment of choice but that solid carbon dioxide and electrodesiccation are also occasionally useful. With 40 per cent of the hemangiomas treatment was followed by no disfiguring scar and there was an excellent cosmetic result. With an additional 47 per cent the results were satisfactory but not perfect from the cosmetic standpoint. With 13 per cent the results were classed as poor, and Ward and Covington grouped these lesions as follows: (1) port wine stains which were radioresistant, (2) hemangiomas in adults and (3) organized remnants, telangiectasia, atrophy or loss of hair.

KERATOSIS BLENORRHAGICA: A BRIEF REVIEW AND REPORT ON THE EFFECTS OF HYPERPYREXIA IN ITS TREATMENT. F. C. COMBES, C. DIETRICH and J. COHEN, J. A. M. A. **114**:2078 (May 25) 1940.

Combes, Dietrich and Cohen review the literature, discuss the symptoms, diagnosis and treatment of keratosis blenorrhagica and report 2 cases of the disease.

They agree with other authors that the most effective therapeutic procedure is the use of fever therapy. In their cases fever was induced by the inductotherm. Success was achieved after chemotherapy with sulfanilamide in one case and a sulfanilamide derivative in the other was ineffective.

RECURRENT HERPES OF THE CORNEA AND RECURRENT HERPETIC FEVER: RESULTS OF TREATMENT WITH SMALLPOX VACCINE. P. L. DAVIS, J. A. M. A. **114**:2098 (May 25) 1940.

Davis reports uniformly successful results in the treatment of recurrent herpes simplex by the use of smallpox vaccine. He treated 3 patients with herpes of the cornea and 11 patients with recurrent herpetic fever. He advises vaccinations every ten to fourteen days for from four to eight times.

USE OF VITAMIN G IN PEMPHIGUS: REPORT OF A CASE OF PEMPHIGUS VULGARIS TREATED SUCCESSFULLY WITH RIBOFLAVIN. M. C. TOPPING and A. F. KNOEFEL, J. A. M. A. **114**:2102 (May 25) 1940.

A white man aged 51, a coal miner, had a generalized eruption which persisted for four months before he was seen by Topping and Knoefel. The diagnosis of pemphigus was unmistakable. Various treatment procedures resulted in no improvement. After the daily administration of 1 Gm. of riboflavin concentrate (containing 970 Sherman-Bourquin units of vitamin G per gram), the lesions began to disappear and at least a temporary remission of the disease occurred.

DERMATITIS FROM ELASTI-GLASS GARTERS AND WRIST WATCH STRAPS. E. P. ZEISLER, J. A. M. A. **114**:2540 (June 29) 1940.

Zeisler reports 2 instances of the development of an acute eczema following contact with elastiglass. In 1 patient, garters made of elastiglass had been worn for three weeks before the rash appeared. In the second patient, the eruption began at the point of contact two weeks after he began to wear an elastiglass wrist watch strap. According to Zeisler, elastiglass is a flexible synthetic resin derived from vinyl resin.

LEWIS, New York.

ERYTHEMA NODOSUM ASSOCIATED WITH ACUTE TUBERCULOUS CERVICAL LYMPHADENITIS. BRIAN C. THOMPSON, Brit. M. J. **1**:159 (Jan. 28) 1939.

Thompson reports 6 cases of erythema nodosum associated with acute tuberculosis of the cervical lymph nodes. In 2 cases the lesions of erythema nodosum developed concurrently with exacerbations of tuberculous infections in the lymph nodes. It is suggested that the lesions of erythema nodosum result from hematogenic tuberculous foci. In 2 cases there were synchronous exacerbation and remissions of tuberculous phlyctenular keratoconjunctivitis and of cutaneous lesions, which is interpreted as further evidence of related allergic phenomena.

THE TRANSMISSION OF SYPHILIS BY BLOOD TRANSFUSION. J. A. W. MCCLUSKIE, Brit. M. J. **1**:264 (Feb. 11) 1939.

This case is the first authenticated instance of transfusion syphilis reported in Britain.

A woman who was delivered by cesarean section of a healthy baby received a transfusion of 800 cc. of her brother's blood on July 2, 1937. The mother's and baby's reactions to Wassermann tests of the blood were negative prior to the transfusion. The donor's blood gave a negative reaction, and examination showed no evidence of infection. The recipient's blood was again tested after the transfusion, and a negative Wassermann reaction was elicited. She was discharged as well on July 24.

On July 13 the donor visited the outpatient clinic for venereal diseases, where he gave a history of exposure to infection six weeks previously. At the time of his visit he had several chancres, in the exudate of which Spirochaeta pallida was found, as well as enlarged inguinal nodes. The Wassermann reaction of his blood was doubtful. Not until September did he volunteer the information that he had acted as a blood donor. On September 11 his sister, the recipient, was examined. She had had jaundice, and there were a few scaly coppery spots on the arms and a slight general adenitis. The Wassermann reaction of the blood was strongly positive, and treatment was instituted.

This case again calls attention to the danger of transfusion syphilis from donors who are in the prechancre stage. To avoid the risk of syphilis by transfusion, it is recommended that only cadaver blood be used.

A Suggested Skin Protective. P. B. Mumford, Brit. M. J. **1**:266 (Feb. 11) 1939.

The ideal protective agent must be easily spread, must remain stable in the presence of most other chemical agents, must provide an oil film of low surface tension, but not be hygroscopic, must be nontransferable, must allow penetration of chemicals through itself, must be able to prevent heat-insulating effect by providing a low surface tension and a capacity to mix with water, must fill hair follicles with an inert but easily removed substance and should be easy to remove without the use of scrubbing brushes or detergents other than good soap.

Such a preparation is known as "HEB protective (waterproof)." The constituents are higher fatty alcohols (palmityl and stearyl), acid esters of these higher fatty alcohols, liquid petrolatum, hydrous wool fat, water and perfume.

Some Aspects of the Venereal Disease Problem in the Federated Malay States. Ian D. Gebbie, Brit. M. J. **1**:438 (March 4) 1939.

The incidence of syphilis and gonorrhea in the Federated Malay States is high and runs roughly in proportion to the racial origin. It is highest in the Chinese, next in the Indians, next in the Malays and lowest in the rest. The great prevalence of malaria probably diverts the medical attention from the treatment of venereal infections. The comparatively small number of medically trained men in relation to the amount of work to be done is also a factor in the high incidence.

The living conditions of the Chinese laborers is poor. The men greatly outnumber the women, and prostitution is rife. Since the populations of the towns average over 50 per cent Chinese and prostitution is most prevalent in the urban areas, the spread of venereal disease in the Chinese is rapid. The Indians form only about 20 per cent of the urban population and work mostly in the country. Their conditions are much more sanitary, particularly on the large estates. The Malays are mostly rural dwellers and form roughly only one tenth of the urban population, and the sex ratio is more natural; hence prostitution and promiscuity are much less than among the Chinese and Indians, and the incidence of venereal disease is therefore much less.

The treatment of venereal diseases at special clinics with the direction of the work against venereal disease by a specialist officer was abolished in 1936. This resulted in a very low basis of standards. The clinics were dirty and ill kept. The amount of treatment given was very low, averaging only four and seven-tenths injections of arsphenamine or bismuth per case of syphilis. In a clinic serving a population of 60,000 there were no facilities for dark field examination of suspected primary lesions and it was necessary to wait for the development of positive serum reaction before treatment was instituted.

Since the introduction of more intensive educational programs there has been an increase in the tendency to regard these diseases as social stigmas which demand secrecy in their treatment. Not until 1930 were brothels closed by governmental action. At that time, of 2,541 women who were treated in Kuala Lumpur 1,637

were prostitutes. In the state of Perak one district was studied in which every male Indian coolee, 950, was tested, and approximately 10 per cent gave positive Wassermann reactions. Leprosy, yaws and malaria were ruled out in these cases. Positive Wassermann reactions were found in approximately 10 per cent of a large group of Indian women, and in a large number of Chinese the rate was approximately 16.6 per cent. It is thus shown that social conditions have a direct relation to the prevalence of venereal disease.

SEVERE SKIN AND GENERAL REACTION FOLLOWING THE ADMINISTRATION OF M & B 693 AND EXPOSURE TO ULTRA-VIOLET LIGHT. RUPERT HALLAM, Brit. M. J. **1**:559 (March 18) 1939.

The author reports a case which demonstrates the photosensitizing action of sulfapyridine. A man aged 25 who had been taking the drug for four days for acute urethritis received a three minute exposure from a standard mercury vapor lamp at 40 inches (102 cm.) to the back and front. Five days later he was admitted to the hospital suffering from extensive extremely painful second degree burns. He was generally ill, with a fever and rapid pulse. The skin was edematous and covered with many crusts, and there were many bullae in the mouth. He eventually made a complete recovery. It is pointed out that an exposure to ultraviolet radiation precipitated the onset of this intense reaction as a result of photosensitization of the skin. Every patient should be expressly warned of exposure to sunlight or to artificial radiation during the time he is taking this remedy.

APPEL, Boston.

ON THRUSH, WITH SPECIAL REFERENCE TO VAGINAL THRUSH. W. GLEN LISTON and LEWIS G. CRUICKSHANK, Edinburgh M. J. **47**:369 (June) 1940.

The authors begin with the statement that "any housewife knows that thrush is a condition which affects the mouths of suckling infants and old persons suffering from debilitating diseases."

There is first a discussion of the parasite of thrush as to nomenclature and differentiation from other organisms. Oidium albicans is the cause of thrush, whether it occurs in the vagina, the mouth or the skin.

The authors report 49 vaginal infections in a series of 200 consecutive pregnant women suffering from leukorrhea. The diagnosis is suggested by the history; thrush is seldom diagnosed by any vulvar manifestations but is discovered by examination of the vagina by speculum. Films were made and stained by the Gram method. The technic of examining films is thoroughly discussed.

The disease should be sought in the pregnant mother in order to safeguard the baby from infection at birth.

TRANSFUSION-SYPHILIS WITH WIDESPREAD OSTEOMYELITIS AND CUTANEOUS LESIONS OF AN ERYTHEMA MULTIFORME TYPE. H. C. PIAN and C. N. FRAZIER, Chinese M. J. **57**:301 (April) 1940.

The authors report on 2 Chinese patients, 1 a boy of 8 years, who were recipients of blood from a professional donor of three years' experience. The donor had no physical indications of disease and a negative Kline reaction of the blood immediately before the two transfusions.

Syphilitic lesions developed in the recipients. The donor was then reexamined, and it was learned that twenty days after the transfusions a penile sore had developed. The blood test gave a positive reaction.

Roentgenograms of 1 of the recipients before treatment showed syphilitic destruction of bone in the skull and long bones, and five months after treatment demonstrated the healing of the lesions, with residual thickening of the periosteum and the cortex.

The second recipient had multiple lesions of the periosteum and a rash resembling erythema multiforme.

The writers discuss the procedure for prevention of such a catastrophe and also the effect of the size of the inoculum and the route of the infection on its virulence. NEFF, Kansas City, Mo. [AM. J. DIS. CHILD.]

GENERALIZED PUSTULAR PSORIASIS HEALED BY EOSIN. H. GOUGEROT and CIVATTE, Bull. Soc. franç. de dermat. et syph. **46**:1448 (Dec.) 1939.

The patient was a woman aged 58 who during seventeen years had had five attacks of psoriasis, each of which had followed a violent emotional shock. The last outbreak was most severe; the eruption was practically generalized and pustular in type. There were general malaise, chills and fever. Separate areas were treated with salicylated petrolatum, potassium permanganate, chrysarobin and eosin. The therapeutic action of eosin was far superior to that of the other remedies.

A NEW CASE OF RHABDOMYOMA OF THE TONGUE. A. CIVATTE and M. DUCOURTIOUX, Bull. Soc. franç. de dermat. et syph. **46**:1458 (Dec.) 1939.

The authors call attention to the rarity of rhabdomyoma of the tongue and report a case of the condition in a woman aged 35. The tumor was situated on the margin of the tongue and was 2 by 1 cm. The yellow color suggested xanthoma. The lesion was firm and its surface smooth. Histologically, the tumor was characterized by collections of large clear cells interspersed with collagenous and striated muscle fibers. The oval or round tumor cells had well stained nuclei situated in a large mass of clear granular cytoplasm. LAYMON, Minneapolis.

LATE HEREDITARY SYPHILIS OF THE TESTICLES. J. GAZZOLO, Rev. méd. latino-am. **25**:1367 (Sept.) 1940.

The author reports a case of a boy of 14 years with a history of bilateral interstitial keratitis who was brought to him because of a firm, uniform, painless enlargement of both testicles. The child presented typical Hutchinson teeth and opacities of the corneas. The boy was given mercury and iodides by mouth and intramuscular injections of a bismuth compound, and there were rapid improvement in the testicular condition and complete return to normal.

ACNE VULGARIS AND CARBOHYDRATE METABOLISM. M. F. BLANCO, E. E. FONGI and A. BOTBOL, Rev. méd. latino-am. **26**:36 (Oct.) 1940.

In 21 cases of juvenile acne the fasting values for blood sugar were found to be normal in all. Sugar tolerance curves were normal in 52 per cent and slightly below normal in 45 per cent, and in only 1 case was there an abnormally elevated curve. After a high carbohydrate regimen sugar tolerance curves were generally lower, which is normal for nondiabetic persons. It was the authors' impression that a high carbohydrate regimen benefited a certain number of the patients and that in no instance was it definitely harmful. They stated the belief that the frequent observation of abnormally low sugar tolerance curves (45 per cent) is of some significance. LEIFER, New York.

GUMMA OF THE LIDS AND CONJUNCTIVA. A. LIPOVSKAYA, Vestnik oftal. **15**:88, 1939.

That gummatous involvement of the lid or conjunctiva is rare is indicated by the fact that during a period of twenty-six years only 8 persons with such a condition were observed among 219,139 patients. Reports are given of 3 patients seen

within a short period in 1936 in the university ophthalmic clinic of Kuban (Caucasus).

CASE 1.—A man aged 47 had an ulcerated lesion on the conjunctiva of the upper lid of the left eye which was diagnosed as tubercle of the conjunctiva because of the appearance and because of the history of recurrent pleurisy and pneumonia. After the Wassermann reaction of the blood was found to be positive, he was given antisyphilitic treatment, and the ulcer on the conjunctiva and a similar one on the shoulder healed, leaving a scar, so that the diagnosis was changed to a gumma of the conjunctiva.

CASE 2.—A woman 37 years old complained of a persistent "stye" of the lower lid of the left eye for several months. The margin of the lid was ulcerated and the lid swollen. The condition could be taken for either an epithelioma or a tuberculous lesion. The Wassermann reaction of the blood was positive, and the ulcer healed after one course of antisyphilitic treatment. The character of the ulcer indicated tertiary syphilis.

The third case was interesting because interstitial keratitis developed in addition to the cutaneous lesion in the region of the brow, both conditions being part of tertiary syphilis. Since interstitial keratitis developed later in the other eye, the disease was evidently congenital syphilis. O. SITCHEVSKA. [ARCH. OPHTH.]

THE OCCURRENCE OF SOLAR-DERMATITIS IN LYMPHOGRANULOMA INGUINALE. C. E. SONCK, Acta dermat.-venereol. **20**:529 (Sept.) 1939.

The author observed 42 cases of solar dermatitis among 100 women with lymphogranuloma venereum. In some cases the eruption lasted a few hours only. In others it persisted for several days after exposure to the sun. The eruption consisted of bright red papules, which sometimes coalesced and formed large patches. Vesicles were also seen in some cases. In some cases the sunlight increased the intensity of the Frei reaction. In a patient who had a solar dermatitis the healed site of a Frei reaction flared up, again becoming, so to speak, "positive." The author thinks that perhaps some sensitizing substance is developed in patients with lymphogranuloma venereum or that there is an increase of certain photosensitive elements (proteins or lipoids) in the blood serum or in the skin.

PROFESSIONAL DERMATOSES AND THEIR COMBATING. J. STRANDBERG, Acta dermat.-venereol. **20**:613 (Sept.) 1939.

The social importance of dermatoses due to occupation and the question of the value of different kinds of allergic tests, especially patch tests, are discussed. The possibility of delayed reactions has to be taken into consideration, and daily readings for five to six days are advised before a negative result is reported. The possibility of a negative phase caused by temporary desensitization and also the variation of the hypersensitivity of different areas of the skin is mentioned. Polyvalent hypersensitivity may be observed sometimes, and that renders the evaluation of the patch test much more difficult. The author suggests that scientific research into the means of combating occupational dermatoses should be entrusted to the dermatologic clinics.

ETIOLOGICO-PATHOGENETICAL EXPERIENCES OF PROFESSIONAL SKIN DISEASES WITH A VIEW TO THEIR PROPHYLAXIS. POUL BONNEVIE, Acta dermat.-venereol. **20**:632 (Sept.) 1939.

Bonnevie classifies the external causes of occupational diseases of the skin as (1) physical, (2) chemical and (3) infectious. The physical influences are: mechanical traumas, heat, cold, light, electricity, ultraviolet rays, roentgen rays and radium rays. Acutely provoked changes in the skin caused by physical influences may pave the way for other influences. The control of labor accidents may be a direct contribution to the prophylaxis of trade diseases.

The author discusses sensitizations which may follow physical influences, especially in the presence of an individual predisposition. Different chronic physical irritants seem to play an important part in the development of cancer. The chemical influences may produce necrotizing processes, toxic dermatoses, inflammatory processes of eczematous and noneczematous character, chronic degenerative changes and also hyperplastic processes.

Occupational infections of the skin may include infections by pyococci or fungi, infections derived from animals and other conditions which present a predisposing cause for sensitization eczemas. The author believes that the allergy in idiosyncratic eczema seems to be connected in principle only with antibodies contained in the epithelial cells. The presence of the antibodies is due to the preceding activity of antigens. Idiosyncratic eczema can be described as a combined exposure and sensitization disease. This condition may pave the way for new sensitizations.

In prolonged periods of continued contact with a substance there may be a certain "time of exposure" before the beginning of the period of sensitization. In some cases the hypersensitivity develops only after several weeks, months, years or even decades. The different chemical substances are of varying sensitizing ability. The author believes that the prophylaxis of eczema will be facilitated by the discovery of active noxae and their substitutes.

VITAMIN C AND SKIN DISEASES. P. HANSEN and P. BRAESTRUP, Acta dermat.-venereol. **20**:676 (Sept.) 1939.

The authors studied the possible relations between cutaneous diseases and ascorbic acid (vitamin C) in 24 cases of various diseases (psoriasis, pemphigus, erytheroderma, dermatitis herpetiformis, eczema and others). The content of ascorbic acid in the blood was examined before and during the intake of different doses of ascorbic acid. A table illustrating, among other data, the various values of plasma ascorbic acid and the various doses of ascorbic acid administered in each case is attached. The authors claim that the administration of ascorbic acid did not have any influence on the course and the duration of the cutaneous diseases in the cases observed.

ASTRACHAN, New York.

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

LEO SPIEGEL, M.D., *President*

HENRY SILVER, M.D., *Secretary*

Dec. 26, 1940

Nicotinic Acid Deficiency Secondary to Removal of a Portion of the Gastrointestinal Tract. Presented by DR. PAUL GROSS.

D. V., a white man aged 51, had an eruption in the right axilla which developed in October 1931. During the following year it gradually spread to involve the face, chest and abdomen. The application of various lotions and salves was followed by temporary improvement. In 1937 the ankles became involved. At this time the patient was seen at the Vanderbilt Clinic, where a diagnosis of seborrheic eczema was made. He had a fine scaly eruption around the eyes and around the umbilicus. The skin of the upper part of the sternal region and in the right axilla was erythematous and oozing. There was also an erythematous papular eruption involving the ankles.

In June 1931 he was operated on at the Presbyterian Hospital. Eighteen centimeters of the upper portion of the ileum was removed. The microscopic diagnosis was carcinoma of the ileum. There has been no evidence of recurrence of the malignant growth.

In October 1940 Dr. J. G. Hopkins and I suggested the diagnosis of seborrheic-dermatitis-like eruption possibly due to a vitamin deficiency. On October 23 the patient was given 50 mg. of nicotinic acid three times a day. On November 6 his face had cleared completely.

Examination of the blood showed 100 per cent hemoglobin, 4,940,000 erythrocytes and 7,200 leukocytes, with 62 per cent polymorphonuclear leukocytes, 30 per cent small lymphocytes, 2 per cent large lymphocytes and 6 per cent eosinophils.

The coenzymes I and II of the blood were normal. The amount of coproporphyrin in the urine was 0.188 mg. before hydrolysis and 0.228 mg. after hydrolysis.

Pityriasis Rubra Pilaris and Vitamin Therapy. Presented by DR. PAUL GROSS.

R. L., a white man aged 39, was presented before the Bronx Dermatological Society on Oct. 24, 1940 (ARCH. DERMAT. & SYPH. **43**:751 [April] 1941). He is again presented to demonstrate the effect of vitamin therapy.

During September and October the patient received 150 mg. of nicotinic acid per day, resulting in improvement of the general condition and also of the follicular keratosis. The treatment was then combined with the administration of yeast concentrate. The psoriasiform lesions, however, failed to respond. The addition of pyridoxine, 20 mg. per day, and riboflavin had no effect on these lesions. Since December 4 the patient has been receiving yeast concentrate again and has shown further improvement of the hyperkeratosis on the palms and of the follicular keratosis on the elbows.

DISCUSSION OF VITAMIN THERAPY

DR. GUSTAV J. MARTIN (by invitation): I should like to discuss the vitamins A and C in the light of newer knowledge. Beta carotene is an aliphatic methyl-

ated hydrocarbon having two identical unsaturated, optically inactive terminal rings. The carotene structure is evidently capable of hydrolysis at the aliphatic polyene central chain, giving rise to two identical half beta carotene alcohols. The ring structure, the unsaturated, polyene chain and the aliphatic primary alcohol group are all of major importance in the biochemistry of vitamin A. The unsaturated, unoxidized, optically inactive ring evidently plays some important role because only carotenoids having the ionone ring can be converted into vitamin A. The side chain unsaturation explains the most probable function of vitamin A as an oxidation-reduction catalyst. The alcohol structure in vitamin A explains its ability to form compounds with fatty acids, proteins and bile acids, all of which are evidently important in its biochemistry, namely, the absorption of the vitamin from the intestine as a bile acid compound, its transportation in the blood and lymph as fatty acid esters, its storage in the liver as a fatty acid ester and the apparent occurrence of protein vitamin A compound as a precursor of the visual purple of the retina.

There are certain complications in the determination of vitamin A in biologic materials. The esters of vitamin A are reported to have a greater biologic activity; cyclized vitamin A has no vitamin action and gives the same absorption pattern, and, finally, the oxidation products of vitamin A give the same patterns with or without the antimony trichloride reaction.

The question of hypervitaminosis A has been frequently raised in the past few years. A new approach to this problem lies in the recent report that large amounts of vitamin A produce hypoplasia of the thyroid gland with an increase in the amount of thyrotropic hormone in the anterior lobe of the pituitary gland. This approach may lead to some definite contraindications for the use of massive doses of vitamin A.

Vitamin C plays an important part in resistance, possibly through its action in detoxication. The protective action of ascorbic acid against drug sensitizations and toxicities of all types has been amply demonstrated. I should like to point out an extension of this approach, namely, through prophylactic and therapeutic detoxication generally. The toxic effects of arsphenamine and of many other compounds has been demonstrated to be decreased by the concomitant administration of aminoacetic acid or of a high protein dietary regimen. This focuses attention on the general processes of detoxication. These are never specific, nor do they ever proceed by a single channel. Specifically, the use of ascorbic acid to decrease sensitization and toxic reactions to arsphenamine is but one of several procedures that could be adopted. A combination of aminoacetic acid, ascorbic acid and a high protein diet proves more efficacious than ascorbic acid alone. In animals it has been demonstrated that the use of several compounds in combination by the body in the usual processes of detoxication protects to the greatest extent against the toxic and lethal action of arsphenamine. Ascorbic acid, aminoacetic acid, calcium glucuronate and cystine all protect in some measure against the lethal action of arsphenamine in mice.

Dr. Klaus Unna (by invitation), Rahway, N. J.: I should like to take up the question of the vitamin B complex. In the course of work on concentration and isolation of vitamin B from natural sources and research on vitamin B deficiency in species other than the chick, it became evident that vitamin B is not a single chemical entity but is of multiple nature. The rapid progress in the resolution of the vitamin B complex during the last years is due to the combined efforts in clinical investigation, in studies of experimentally controlled deficiency diseases in animals and in the chemical isolation of the active substances in pure form from natural sources. The vitamin B complex today includes all water-soluble vitamins other than vitamin C. Yeast, rice polishings and liver are the richest sources for most of the members of the vitamin B complex.

Deficiency diseases characterized by dermatitis develop in both rats and chicks on diets containing thiamine and riboflavin but otherwise free from the vitamin B complex. The diseases rat acrodynia and chick dermatitis were long thought to be caused by the lack of the pellagra-preventive factor (nicotinic acid), which is

responsible for human pellagra and black tongue disease in dogs. It is now known that rat acrodynia and chick dermatitis are caused by the lack of two different vitamins. P. György (*J. Biochem.* **29**:741, 1935) offered the first experimental proof that rat acrodynia is due to the lack of a new heat-stable factor other than riboflavin or nicotinic acid, which he named vitamin B_6. Later it was shown that pyridoxine (vitamin B_6) is essential for the nutrition of chicks, pigs and dogs. On a diet free from pyridoxine, dogs have a microcytic hypochromic anemia which does not respond to iron but is readily cured by pyridoxine. Lesions appear after four to six weeks on diets free from pyridoxine and consist in a florid dermatitis localized on the paws, the ears and the snout. Ulcers are frequently found around the snout and under the tongue. The administration of crystalline pyridoxine in microgram doses readily cures these lesions.

Pantothenic acid, first discovered as a growth factor for yeast, was found to prevent and cure the so-called chick dermatitis. The rat also needs pantothenic acid. Rats on synthetic diets supplying adequate amounts of thiamine, riboflavin, nicotinic acid and pyridoxine cease to grow after three to four weeks and have scant and coarse fur with scaliness of the skin and blood-tinged whiskers. On autopsy adrenal hemorrhages are frequently found. These lesions are prevented or cured by the administration of 100 micrograms of pantothenic acid per day. Recently, for the first time, my associates and I have obtained litters from rats raised on a strictly synthetic diet supplemented with vitamins in crystalline form. This does not imply that there are no more unknown factors in the vitamin B complex. It indicates, however, that if there are they are not essential for maturation and reproduction of rats.

Another interesting observation on pantothenic acid is its striking effect on nutritional achromotrichia. In young black rats maintained on a diet free from pantothenic acid, in addition to the already mentioned deficiency symptoms, iron gray or silver gray fur develops. The graying develops in symmetric patterns on the body. Administration of pantothenic acid restores the black color of the fur within four to five weeks. If pantothenic acid is present in the diet the animals do not get gray hair.

It should be kept in mind that vitamin deficiencies affect first and primarily the metabolism in general; when there are deficiencies of the B vitamins the carbohydrate metabolism and the fat metabolism are affected. The deficiency symptoms observed are only the consequences of a severe metabolic derangement. Furthermore, the lack of a vitamin produces entirely different symptoms in different species of animals. Nicotinic acid deficiency, for instance, causes black tongue disease in dogs and pellagra in man but apparently does not harm chicks or rats. Pyridoxine deficiency causes a characteristic dermatitis in rats; in dogs, however, it produces severe hematologic changes. Therefore, the observation of certain deficiency lesions in one animal species does not imply that other species or man will be similarly affected. As helpful and fundamental as investigations on experimental deficiencies in animals are for the expansion of the knowledge of vitamins, the clinician's art and skill in observing and treating patients, in addition to this knowledge, will always be required to establish the symptomatology of single or multiple deficiency diseases.

DR. MARION B. SULZBERGER: There are important questions with which all dermatologists are faced when they attempt to treat dermatoses by administering vitamins. Many of these questions have already been mentioned by Dr. Martin and Dr. Unna. They too, however, conveyed the impression that the majority of these practical questions were yet to be answered.

Of practical importance is the question whether there is a difference in the effects of the natural vitamins, i. e., vitamins as they occur in nature, and of the synthetic products. The impression is that the natural products may in some ways be superior to their synthetic analogons. Is there, for example, a difference between the effect of natural vitamin D as obtained from fish oil and that of the irradiated sterols, such as the irradiation product of ergosterol used in viosterol in oil and dihydrotachysterol? Is it not conceivable that impurities which may be

present in traces in natural products are of some importance in their therapeutic effects? Is there not some unknown factor in yeast or in liver which is an important adjunct to the vitamin B complex?

A second question is whether the combinations or the ratio of one vitamin to another may not be of importance, as, for instance, the ratios of thiamine, riboflavin, nicotinic acid and pantothenic acid to each other and to other factors of the vitamin B complex. In the light of clinical observations, it cannot be a matter of indifference as far as vitamin demand is concerned whether a person has a high or low intake of protein, fat or carbohydrate in the diet. The correctness of these statements is evidenced, for example, in the fact that starving populations, in whom the total caloric intake is reduced or the number of fat calories is reduced in some proportion to the reduction of vitamin intake, do not, as a rule, present manifestations of certain vitamin deficiencies in the proportion in which one would expect to see them.

A further question of interest is the great variation in the requirements of particular vitamins on the part of various species or races and on the part of various tissues, organs or parts of organs. Thus, for example, certain human beings may have requirements for particular vitamins to a much greater degree than others. Here many known and unknown influences play a part. I may mention (1) hereditary and constitutional factors determining faulty absorption, transportation or utilization or increased local requirements of certain vitamins or (2) acquired disturbances, e. g., gastrointestinal factors and interference with absorption. Moreover, human beings are, in all probability, inclined to vary in the demands of their different organs, so that in one person vitamin A deficiency will first become apparent in the eyes in the form of defective light-dark adaptation and in another the same degree of dysvitaminosis will manifest itself at first in the appearance of a dry skin with follicular keratoses.

As Dr. Unna pointed out, in the nutritional achromotrichia of the rat, one finds that the reduction in the responsible vitamins produces a graying of the hair of certain parts of the body but not of the hair of the head and that different parts of the hairy covering thus must have entirely different requirements for the vitamin concerned.

To follow Dr. Unna further, it would seem that almost each person may display his own particular standards and quantitative demands for various vitamins, so that one might liken one human being to the guinea pig in his tendency to have scurvy, another to the dog in his tendency to have blood dyscrasias or lesions of the mucous membranes and still another to the rat in his tendency to have dermatitis of various kinds. This, of course, is more a pictorial way of bringing home this point than an actual scientific analysis. Nevertheless, I believe that it illustrates well the fact which must be recorded as an established truth, namely, that certain persons, certain organs and certain parts of organs will be much more susceptible than others to the slightest upsets in their normal vitamin supply.

I wish to emphasize that the manifestations which are observed in the skin or in other organs—the dysvitaminosis—are simply "end results," which can differ in different persons. These end results can be produced through an intermediate mechanism, such as a metabolic disturbance, a local or general nervous mechanism, a reduction of resistance, an immunologic upset or, above all, an influence on the endocrine glands and the functions they control.

I should like to relate my experience and that of my associates, Drs. Joseph Goodman, Naomi M. Kanof and Rudolf L. Baer. In cases of dryness of the skin, including instances of what seemed to be a mild form of ichthyosis and, in particular, instances of keratosis follicularis, the condition has improved by the administration of large doses, from 30,000 to 500,000 and more U. S. P. units per day, of vitamin A over periods of several months. Benefits from this form of therapy were observed also in brittleness of the nails. Still another effect was noted in some cases of dryness and brittleness of the hair, the hair resuming its normal sheen and appearance under vitamin A therapy. The condition known as Sjögren's syndrome, which resembles the somewhat better known Plummer-

Vinson syndrome, was not benefited by the administration of iron or of most vitamins, but it was benefited when vitamin A was given. Another condition in which vitamin A therapy has proved of benefit is lichen spinulosus with folliculitis decalvans, as first described by Graham Little (Editorial, in Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1938).

Before leaving the subject of my own observations on the therapeutic applications of vitamin A, I should like to point out two important facts, the first of which is the apparent interrelation between vitamin A and the effect of thyroid. Both of these substances have been shown to be beneficial in certain cases of the triad of dry hair, brittleness of the nails and dry skin with follicular keratoses. This illustrates the fact to which I previously alluded concerning the intimate relation between hormones and the effects of vitamins on metabolism. The second feature which I consider of great interest is the relation seen in Sjögren's syndrome between malignant epithelial changes and a deficiency of vitamin A.

Regarding the vitamin C deficiencies, aside from the scorbutic manifestations, follicular hyperkeratosis and dry skin, which are helped by vitamin A in many cases, are in other cases more benefited by large doses of vitamin C. The effect of intermediate doses of vitamin C in preventing cutaneous sensitizations of guinea pigs to neoarsphenamine is of interest. I am in hearty agreement with Dr. Martin's remark that vitamin C surely was not the only factor tending to produce adequate forms of resistance to this sensitization. As a matter of fact, R. L. Mayer and I (Sensitizations, ARCH. DERMAT. & SYPH. **24**:537 [Oct.] 1931), as well as B. Oser and I (*Proc. Soc. Exper. Biol. & Med.* **32**:716, 1934), are of the opinion that vitamin C plays only a small part in increasing the guinea pig's resistance to neoarsphenamine sensitization. We have reason to believe that there must be in green alfalfa another factor or other factors which are much more important than vitamin C in reducing the susceptibility of the guinea pig's skin to sensitization with neoarsphenamine. Moreover, we are not at all certain whether this reduction of susceptibility is really a basic immunologic effect or one which is related only to the particular compounds we studied, namely, neoarsphenamine and paraphenylenediamine. Since vitamin C has such a potent effect on oxidation-reduction potentials, it seems possible that the effect of vitamin C in our animals was related to its influence on the oxidation of the particular allergens studied. I cannot go into further details regarding vitamin C and its effects on cutaneous pigmentation or its relation to the adrenal cortex. Suffice it to say that in cutaneous pigmentation there seems to be a system in which vitamin C, a certain ferment, or certain ferments, the metallic ion of copper and natural promelanin all play an integral part.

To sum up, it may be said that while vitamin therapy is undoubtedly of great promise and while a productive era in dermatology is certainly just beginning in its relation to vitamins, many complications present themselves to the clinician, and many questions must be answered before a general rational application of vitamin therapy can be hoped for in dermatology. The practical yield has thus far been small; nevertheless, a sufficient number of conditions are already known which can be benefited at least to some degree by the administration of the proper vitamins.

DR. PAUL GROSS: The remarks made by Dr. Sulzberger are pertinent and show the problems with which the clinicians are confronted. I have been interested in the Plummer-Vinson syndrome ever since Dr. Rhoads referred to the occurrence of kraurosis vulvae in this disease. This led to the use of vitamin B complex in the form of liver extract for the treatment of kraurosis vulvae.

In reviewing the recent literature, it becomes evident that microcytic anemia and atrophy of the mucous membrane of the mouth and pharynx, associated with epidermal dysplasia, are prominent features of the syndrome. Ahlbom (*Brit. M. J.* **2**:331 [Aug. 15] 1936) showed the important role which the Plummer-Vinson syndrome and achlorhydric anemia play as precursors of postcricoid carcinoma. Ahlbom also described lesions of the angles of the mouth, brittleness of

the nails and occasionally koilonychia as part of the syndrome. Swift (*J. Obst. & Gynaec. Brit. Emp.* **43**:1053 [Dec.] 1936), who studied 43 cases of kraurosis vulvae in relation to achlorhydria and hypoacidity, referred also to the frequency of brittleness of the nails and in 1 case the occurrence of koilonychia. Swift reported good results by correction of the gastric dysfunction and administration of vitamin A. I have, accordingly, in recent years, treated patients with kraurosis vulvae with vitamin A, riboflavin and liver extract, considering the disease as a possible combined deficiency. I may cite another example of the relation between vitamin A and vitamin B deficiency. For a number of years, Dr. George Andrews and I have observed cases of extensive eruptions clinically indistinguishable from pityriasis rubra pilaris and diagnosed as such at dermatologic conferences. The objection to the diagnosis of pityriasis rubra pilaris was the absence of lesions on the back of the fingers and the duration, which varied from a few months to a few years. We have achieved complete cures in several of these cases by intensive treatment with injections of liver extract.

Brunsting and Sheard (Dark Adaptation in Pityriasis Rubra Pilaris, ARCH. DERMAT. & SYPH. **43**:42 [Jan.] 1941) have recently reported good results in pityriasis rubra pilaris with vitamin A therapy. The patient I presented tonight has a typical pityriasis rubra pilaris of long standing, and only because of subnormal amounts of codehydrogenases in the blood I saw an indication for nicotinic acid therapy. There was a definite response in the patient's general condition and a decrease of the follicular keratosis. Pyridoxine (vitamin B_6) and riboflavin had no effect, but large doses of yeast concentrate again improved the condition.

I enjoyed Dr. Unna's fine analysis of the vitamin B complex. For good reasons he did not discuss the anti-pernicious-anemia factor and biotin. Yet biotin (vitamin H) has been of considerable interest to the dermatologist. Its action in the rat has been demonstrated on the dermatitis produced by the raw egg white damage. This is at present the only way to inactivate biotin in the rat and thus produce a deficiency. A spontaneous biotin deficiency, however, has recently been demonstrated in the chick, in which a dermatitis, different from that due to pantothenic acid deficiency, develops. Even in vitro the action of raw egg white on biotin has been demonstrated. The older reports on biotin therapy in dermatology are not encouraging, but further work will have to be done when crystalline biotin is available in therapeutic quantities. György has shown a higher efficiency of the parenteral injection of biotin compared to oral administration, and it might well be that some of the results with injections of liver are due to the biotin effect, although it is supposed to be present only in the residue following liver extraction.

Another member of the vitamin B complex which deserves special attention is pantothenic acid. It is present in very small amounts in foods containing the vitamin B complex, and its full therapeutic action depends on fairly large doses.

Dr. Unna referred to the relation of the vitamin B complex to carbohydrate and fat metabolism and to the enzymes of biologic oxidation. This is particularly interesting in view of the fact that P. G. Unna, his grandfather, many years ago realized and stressed the importance of oxidation in the skin. I agree that the cutaneous manifestations in vitamin-deficient animals are the expression of metabolic disturbances and that the results may vary according to species. Therefore, one should not be misled by animal experiments to believe that the vitamin which cures alopecia in the rat will do likewise in the human being.

There may be a relation between generalized eruptions resembling pityriasis rubra pilaris, seborrheic eczema and certain types of pellagra because of their response to vitamin B therapy (Gross, P.: Nonpellagrous Eruptions Due to Deficiency of Vitamin B Complex, ARCH. DERMAT. & SYPH. **43**: [March] 1941).

DR. SAMUEL M. PECK: For some time Dr. Chargin and I have been studying keratosis follicularis from the point of view of its being due to vitamin A deficiency. We believe that our studies might throw additional light on the cause of this disease (Peck, S. M.; Chargin, L., and Sobotka, H.: Keratosis Follicularis [Darier's Disease], ARCH. DERMAT. & SYPH. **43**:223 [Feb.] 1941). We have observed that the blood of patients with keratosis follicularis, even though they

were on a normal diet, was deficient in vitamin A, although the carotene levels were within normal limits. When these patients were given 200,000 U. S. P. units of vitamin A per day, and in some instances even more, there was a gradual but constant improvement over a period of months. Coincident with the clinical improvement there was a return of the vitamin A level in the blood to normal. It was interesting to note histologically that the dyskeratoses gradually disappeared and finally only hyperkeratoses remained. Apparently these patients were unable to convert carotene, since their diets, as far as could be determined, contained adequate amounts. Whether in addition there was an inability to utilize or absorb vitamin A is the subject of our present investigation.

Dr. J. Gardner Hopkins (by invitation): Two obvious facts stand out: first, that the subject of vitamin therapy is of tremendous importance to dermatology and, second, that it is still a complicated and difficult subject.

Presentations like those given by Drs. Unna and Martin are needed to incite more clear thinking about the clinical problems. I do not think that one can administer vitamins with any hope of success unless one tries to understand the chemistry and function of them and the type of symptoms produced by their deficiency in animals.

A fact emphasized by Drs. Sulzberger, Peck and others is that the term vitamin deficiency tends to cloud clinical suspicion. Patients rarely have a deficient vitamin intake. Lesions, of course, occur if diets are inadequate, but in most cases the symptoms that will respond to vitamin therapy do not develop because the patient has taken a subnormal amount of the vitamin previously. As an example, it is known that in pernicious anemia deficiency symptoms are due to gastric atrophy which makes it impossible for patients to use a vitamin they ingest. It has been brought out that symptoms of deficiency may be due to something which prevents absorption, such as a lack of bile salts or the intake of liquid petroleum.

There is evidence that a function of some vitamins is to detoxify substances introduced into the body from the outside or produced within. The first patient shown by Dr. Gross is of interest in this connection. The dermatitis responded to nicotinic acid. A loop of the intestine had been side tracked some years before. Barker and Hummel (*Bull. Johns Hopkins Hosp.* **64**:215 [April] 1939) have reported cases of macrocytic anemia in which they suspected the condition was caused by a toxic substance absorbed from such intestinal loops. In a few the anemia disappeared after surgical removal of the loop, and in others the anemia improved after administration of liver extract.

Dr. Samuel Feldman: About twenty years ago dermatologists were just as interested in the endocrine substances as they now are in vitamins. Soon, however, there was reaction in the opposite direction. I recall a patient with keratosis follicularis, who had low blood pressure, in whom excellent results were obtained with adrenal cortex. On the other hand, I should like to point out that the patient with leukoplakia and kraurosis vulvae whom I presented at the November meeting of this society failed to respond to tremendous doses of vitamins but responded rapidly to stilbestrol. In other cases the reverse may be true.

Since there is a similarity of chemical composition and structure between glandular preparations and vitamins, may there not be a complementary action between the two, so that a deficiency in vitamins may be influenced by a deficiency in endocrine products or vice versa? One should not forget the endocrine products when discussing vitamins.

Dr. David Bloom: I was impressed by Dr. Peck's statement regarding the beneficial effect of vitamin A in keratosis follicularis. If this claim should be substantiated in a sufficient number of cases, it would again prove that although a disease may be hereditary it may be favorably influenced by treatment. It would point out again that the science of heredity does not discourage further investigation; the contrary is true. It would be of great interest to examine all the members of the family for hypovitaminosis, which may not always be clinically manifested as keratosis follicularis.

DR. KLAUS UNNA (by invitation), Rahway, N. J.: Dr. Sulzberger raised the question concerning the different diets used for the production of experimental deficiencies and the relation of the constituents of the diet to the vitamins. These problems are the very ones on which both the animal investigators and the clinicians are working at present. There is already some evidence indicating that the requirements for a given vitamin depend on the nature of the diet. It has been shown that with a diet rich in carbohydrates more thiamine is needed to prevent a deficiency than on diets low in carbohydrates. I think the relation of dietary constituents—protein, fat and carbohydrates—to the vitamin requirement needs much more investigation before such hypothetic questions as racial differences in vitamin requirements can be discussed.

I was interested in Dr. Feldman's discussion on hormones and vitamins. I think there is some experimental evidence dealing with this problem. I should like to refer to experiments demonstrating the difference in vitamin B complex requirements in normal animals and those given thyroid. The thiamine deficiency is accelerated by treating the animals with thyroid.

DR. PAUL GROSS: Dr. Hopkins raised the question of nutrition, since in the cases I referred to there was more frequently improper absorption of vitamins than nutritional deficiency. In regard to the toxicity of the vitamins of the B complex, there can be no doubt that they are nontoxic, even in large doses, but there is some clinical evidence that large doses of thiamine hydrochloride administered over a long period may produce a relative deficiency in nicotinc acid due to the increased requirement.

The interesting work of Dr. Peck again shows the importance of proper absorption and utilization of the vitamins, which can be particularly well demonstrated in the formation of vitamin A from beta carotene. From the work of Kimble and Gordon (*J. Biol. Chem.* **52**:128 [June] 1939), it appears that riboflavin may have an important function in the vitamin A mechanism.

In answer to Dr. Feldman, one should confine the term vitamin therapy in pathologic conditions to a systematic and planned administration of sufficient doses of individual vitamins or of a natural complex like liver extract. It is no contradiction if a condition responds to endocrine therapy as well as to vitamin therapy. One can cure senile vaginitis with vitamin A or with estrogen. The interrelation between glandular substances and vitamins is being constantly studied, and the demonstration of adrenal cortex damage by a deficiency of pantothenic acid is only one example.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

GEORGE C. ANDREWS, M.D., *Chairman*

HERMAN SHARLIT, M.D., *Secretary*

Jan. 7, 1941

Mycosis Fungoides. Presented by DR. HENRY D. NILES.

M. W., a man aged 53, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

Twelve years ago an eruption appeared on the arms and then spread to involve the chest, the neck and the back. It has been rather severe for the past four years. The patient has shown definite improvement following injections of sodium arsenate, commencing Dec. 31, 1940.

Scattered over the trunk and extremities are various-sized round and serpiginous areas of erythematous and scaly patches with slight infiltration and no excoriations. Between these areas are islands of normal tissue.

The Wassermann and Kahn reactions of the blood were negative. Mycologic examination of scrapings from the feet and arm showed no organisms. A complete blood count was normal. Histologic examination by Dr. Satenstein confirmed the diagnosis of mycosis fungoides.

DISCUSSION

DR. A. BENSON CANNON: While most of the members undoubtedly think that an eruption of this type is mycosis fungoides, I do not believe that one would be justified in making such a diagnosis without more evidence. The macular, brownish, erythematous, finely scaly and sharply defined patches are strikingly like those seen in parapsoriasis en plaques. There are no tumors or infiltrated plaques, and the shapes are not as one would expect in mycosis fungoides.

DR. FRANK C. COMBES: I agree with the clinical diagnosis of mycosis fungoides in the early infiltrative stage. This man has considerable adenopathy; there is a gland in the axilla about the size of a hazelnut, and I should not be surprised if the condition might fall into the group described by Symmers (*Arch. Path.* **26**:603 [Sept.] 1938) as giant follicular lymphadenopathy. I suggest that the gland in his axilla be removed and examined histologically. Conditions of this kind are amenable to radiation therapy in the early stages. A certain percentage of them go on to become polymorphous cell sarcomas.

DR. SAMUEL FELDMAN: This case brings to mind one I observed three weeks ago. The patient came to me about a year and a half ago with a history of having had his condition for the previous five months. The lesions looked exactly like those of the patient just presented and were accompanied by severe itching. A biopsy was performed by Dr. Satenstein; a histologic diagnosis could not be made from the ordinary specimen stained with hematoxylin and eosin, but there was a suspicion of mycosis fungoides in an extremely early stage. The diagnosis was corroborated by the Unna methylene blue and eosin method and also by the development of tumors on the patient's shoulders and on one elbow. All lesions of the skin disappeared after superficial roentgen ray treatment. The lesion on the elbow did not disappear completely but left a hard mass behind. The patient remained free of cutaneous lesions until his death. Six months after I first saw him a large tumor developed in the abdomen, which rapidly disappeared after a small amount of roentgen ray treatment. He became free of symptoms and improved in general health. Finally, about two months ago, a tumor of the brain developed, which did not respond to treatment, and the patient died. The supposition was that the condition was some form of lymphoblastoma or Hodgkin's disease associated with mycosis fungoides.

DR. FRED WISE: Was the tumor of the brain examined histologically?

DR. SAMUEL FELDMAN: There was no autopsy.

DR. HENRY D. NILES: The clinical diagnosis of mycosis fungoides was made because of the characteristic configuration of the lesions: round, red, scaly patches with islands of normal skin between them. This diagnosis was confirmed histologically by Dr. Satenstein. I presented this case because of certain unusual features: In spite of twelve years' duration there is little infiltration or itching, but there is definite lymphadenopathy. A complete blood count was essentially normal, but I suspected the possibility of incipient leukemia associated with the cutaneous condition. Incidentally, the eruption responded exceedingly well to four subcutaneous injections of a 2 per cent solution of sodium arsenate. This relieved the itching, and the lesions are definitely paler than they were ten days ago.

Lupus Erythematosus Chronicus Disseminatus. Presented by DR. DAVID BLOOM.

M. P., a Negress aged 38, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Aug. 2, 1939 with an eruption of five years' duration. The eruption started on the upper lip and gradually involved the other areas and the scalp.

The upper lip presents a continuous line, ¼ inch (2 cm.) wide, of black pigmentation. The chin, ears, nose and inner canthi of the eyes show similar darkly pigmented spots. The whole anterior aspect of the scalp shows almost complete alopecia, with pigmentation and depigmentation. On the back and on the chest there are slightly raised, mostly flat, pigmented spots, which have been present for about eight months.

Microscopic examination of the affected skin of the upper lip showed the pathologic structure of lupus erythematosus in the early degenerative stage, and examination of a lesion from her back showed "superficial dermatitis."

A complete blood count, including the differential count, was normal. The urine was normal, and the Wassermann reaction of the blood was negative.

Treatment consisted of twelve injections of a vaccine prepared from a culture of material from the throat, which contained the alpha streptococcus and Micrococcus catarrhalis. She also received one injection of bismuth subsalicylate.

DISCUSSION

Dr J. Gardner Hopkins: The interesting feature of this case is the extraordinary blackness of the pigment. I should like to ask the presenter whether the pigment was proved to be melanin or whether it might possibly have resulted from some previous treatment.

Dr. Louis Tulipan: The pigment might not be melanin. When I asked the patient what kind of injections she had received, she said five of a bismuth compound and thirty-eight of gold sodium thiosulfate before she was treated at the Skin and Cancer Unit, and I believe that this treatment might be the cause of the pigment. Of course, in a piece of tissue large enough to submit to spectroscopic examination, that might be proved. I believe the pigment is due to the gold or the bismuth.

Dr. Henry D. Niles: I think it is interesting to see such an extensive lupus erythematosus, a condition which is considered to be associated with photosensitivity, in a Negro. This disease occurs relatively rarely in Negroes. In cases in which I have seen the condition it has been characterized by a definite pigmentary disturbance, either hyperpigmentation—as in this case—or, more often, depigmentation. I believe that in a Negro lupus erythematosus may cause hyperpigmentation by itself, regardless of therapy.

Dr. E. William Abramowitz: I have seen several Negro patients in whom pigmentation developed at the site of lupus erythematosus even before they received any kind of treatment. This patient presents an unusual deep pigmentation of the skin which is found not only in the patches of lupus erythematosus but in the mouth. I am not certain whether there were patches of lupus erythematosus in the mouth, but one does see hyperpigmentation in the mouth of some Negroes that is of a nevoid nature. The absence of a bismuth line on the gums in my opinion excludes bismuth pigmentation of the face or mouth.

Dr. Eugene Traub: I agree with what Dr. Abramowitz has just said and should like to draw attention to one feature of the case which I believe I am correct in noting: There are really two kinds of discoloration. In the discoloration involving the upper lip the color is entirely in the scaling and crusting, which is almost hypertrophic. On the removal of these scales and crusts I think an area of depigmentation would be discovered, as there are several areas where depigmentation already may be seen. Thus, what seems to be hyperpigmentation in this patient actually proves to be depigmentation of the skin. The other kind of discoloration is true hyperpigmentation, which I believe is probably due to the inflammatory reaction of the disease itself and not to any treatment. Other patients have shown exactly such a reaction prior to the administration of any form of therapy.

Dr. David Bloom: No pigment studies were undertaken in this case, for it was assumed that the pigmentation was due to melanin, as in other cases of

lupus erythematosus. Hyperpigmentation is frequently seen in association with lupus erythematosus, and it is particularly pronounced in Negroes. This patient was shown because of the bizarre appearance of the condition, due to the considerable hyperpigmentation involving the upper lip. The main problem in this case is how to remove this pigmentation and improve her appearance. The depigmented areas on the upper lip are due to the removal of tissue for biopsy and in another spot to the application of solid carbon dioxide.

A Case for Diagnosis (Rosacea-Like Tuberculid of Lewandowsky? Rosacea?) Presented by DR. DAVID BLOOM.

F. S., a woman aged 32, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, with an eruption on the face of three years' duration. The left cheek, near the center of the face, and the nose show erythematous plaques on which are superimposed papules, the size of a pinhead and larger, which are erythematous and show yellowish centers on diascopic pressure. General physical examination revealed no other abnormality, and the family and past histories were essentially normal.

Tuberculin tests elicited a positive reaction to a dilution of 1 : 10,000 but a negative one to a dilution of 1 : 100,000.

Microscopic examination of a papule was reported as "possible rosacea-like tuberculid of Lewandowsky." There was an inflammatory reaction about the hair follicles composed of many round cells, with a few wandering connective tissue cells and giant cells at the base of some follicles.

Rosacea-like Tuberculid of Lewandowsky. Presented by DR. GEORGE C. ANDREWS.

B. M., a woman aged 38, recently consulted me for an eruption localized on the nose and middle part of the face. It first appeared about eighteen months ago as a tiny deep-seated papular eruption on the tip of the nose and has slowly spread to involve the entire cartilaginous portion of the nose and the inner part of the cheeks. There have been no subjective symptoms except occasionally mild itching.

The deep-seated papular eruption is bright red, and some of the lesions are crusted. There are a few small pitted scars about the tip of the nose, and the cartilage feels hard and nodular.

Physical examination showed no abnormalities except the eruption.

The patient's general health has been good. She had measles in early childhood, typhoid fever sixteen years ago and chronic sinusitis eight years ago with crusting about the upper lip. She worked in a tuberculosis sanatorium ten years ago for about six months. There is no family history of tuberculosis.

The injection of a 1 : 1,000,000 dilution of old tuberculin elicited a strong reaction, and the lesions showed much improvement following this test. The Wassermann reaction of the blood was negative, and the urine was normal. Examination of the blood showed: hemoglobin 92 per cent, red blood cells 4,720,000, white blood cells 7,520, polymorphonuclear leukocytes 47 per cent, lymphocytes 49 per cent and monocytes 4 per cent.

The histologic report by Dr. Gerald F. Machacek was as follows: Sections of cutaneous tissue disclosed a specimen which had several pilosebaceous organs. The epidermis showed a localized thinning, edema and leukocytic infiltration. Beneath this area there was a localized infiltration consisting of small mononuclear cells, and in it were dilated capillaries. Focal perivascular infiltration was seen, composed of similar cells. There were also edema, elastosis of the corium and dilated subepidermal capillaries. The changes were suggestive of a leukoblastic process. No evidence of tuberculosis was present. Other considerations were rosacea and an atypical lupus erythematosus. Clinically, the best diagnosis would appear to be rosacea.

DISCUSSION OF ROSACEA-LIKE TUBERCULID OF LEWANDOWSKY

DR. FRED WISE: I discuss these cases with little confidence. The first case does not impress me as one of rosacea-like tuberculid. The condition does not look like rosacea tonight, but it does look as if it might at one time have been a papular eruption resembling rosacea. An acneform papular eruption would show banal inflammatory lesions without characteristic signs of tuberculosis. I think the eruption would respond to white lotion N. F. or to some other mild sulfur treatment. Possibly an analysis of gastric contents to ascertain whether achlorhydria is present should be undertaken with every patient who has an obscure eruption of this type.

In the second patient, I think Dr. Andrews' diagnosis is probably the correct one. The lesions consist of papules smaller than pinheads, especially on the bridge of the nose, and the color is suggestive of the Lewandowsky type of rosacea-like tuberculid. Or one might be dealing with a miniature papular tuberculid instead of the true Lewandowsky type. I do not know which of the two this condition is, but I favor a diagnosis of Lewandowsky's disease. The difficulty in making this diagnosis is that the results of histologic examination do not always correspond to the clinical diagnosis, and even tuberculin tests are not always informative. In some cases of rosacea-like tuberculid there is hyposensitivity to tuberculin, in others normal sensitivity and in still others a high grade sensitivity.

DR. GEORGE C. ANDREWS: I suggest that in a unilateral eruption such as this a roentgenogram be made of the antrum. I have seen such eruptions over an infected antrum.

DR. DAVID BLOOM: In spite of the fact that the histologic picture suggests the possibility of rosacea-like tuberculosis of Lewandowsky, I am not certain about this diagnosis. The papules are larger than those usually described in this disease, and the sensitivity to tuberculin is not as great as would be expected. No focus of tuberculosis could be detected, on auscultation or percussion of the lungs or in the roentgenogram. I am in favor of the diagnosis of rosacea. In order to decide the diagnosis definitely, treatment for rosacea will be instituted, and if the patient does not respond to this treatment, gold sodium thiosulfate will be given, which acts favorably in rosacea-like tuberculosis.

DR GEORGE C. ANDREWS: The last remarks of Dr. Bloom apply strongly to the case I presented. One reason I think the condition is true rosacea-like tuberculid is that the patient was treated with hydrochloric acid and a special diet for months without response. Then I injected a 1: 1,000,000 dilution of tuberculin, which elicited a strongly positive reaction, and in one week the eruption was much better. She is being treated with tuberculin now.

Lupus Erythematosus and Psoriasis. Presented by DR. PAUL GROSS.

E. C. M., a man aged 52, is presented from Vanderbilt Clinic with an eruption on the face, scalp, ears and legs of seven months' duration. The first lesion began on the right cheek near the ear. On both cheeks are large, confluent, somewhat scaly patches, slightly infiltrated with bluish red. The borders of the lesions are sharply defined. Smaller lesions of the same type are on the nose and behind the ears. An erythematous scaly eruption is on the scalp. On the anterior surfaces of the legs are typical lesions of psoriasis.

The Kline and Wassermann reactions of the blood were negative. Analysis of gastric contents suggested a hypoacidity, with the free hydrochloric acid amounting to 24 and the total acid to 30. Urinalysis showed a 2 plus reaction for albumin, with hyaline and finely granular casts. There were 0.133 mg. of coproporphyrin in a twenty-four hour specimen of urine. The hemoglobin content of the blood was 96 per cent, and codehydrogenase determined by factor V for parainfluenza bacilli was present in high normal amounts in the blood corpuscles.

Histologic examination of a small piece of skin disclosed a keratin layer which was definitely parakeratotic. Acanthosis was also pronounced. Rete pegs had undergone elongation and were pale and clubbed. There was edema of both the epidermis and the corium. In the keratin layer localized collections of polymorphonuclear leukocytes were seen. The dermal vessels were thickened. A slight chronic inflammation was present. The lesion was evidently a chronic psoriasiform dermatitis.

DISCUSSION

DR. FRANK C. COMBES: I think every one will agree with the diagnosis of psoriasis on the legs. There might be some difference of opinion regarding the lesions on the scalp, although I think the majority will agree that for these too psoriasis is the correct diagnosis. The scalp has been excoriated to a considerable extent. In reference to the lesions on the face, there will probably be much difference of opinion. The lesions are edematous, and about the ears they are almost weeping. Here the histologic examination suggested lupus erythematosus. On the face lupus erythematosus is not infrequently difficult to distinguish from psoriasis. I think there are two separate conditions in this case, lupus erythematosus of the face and psoriasis of the scalp and legs.

DR. CHARLES WOLF: Do I gather from the history that the entire eruption appeared at the same time?

DR. PAUL GROSS: Yes.

DR. CHARLES WOLF: Is it not unlikely that a patient who had not had a dermatosis prior to this attack would have two diseases simultaneously? The lesions on the face may be explained by the fact that the patient might have been excessively exposed to the sun, which might alter the characteristic appearance of psoriasis. The other lesions seem to be typical of this condition, although there is no stippling of the nails. However, the lesions that are psoriatic are so typical that it is logical to infer that the entire eruption is that of psoriasis. The histologic picture is not definitely that of lupus erythematosus but only suggests that possibility. Edema may occur in psoriasis in the early stages; acanthosis may not be pronounced, as in the later stages, and other histologic criteria may be absent. So, on the strength of one examination I prefer the diagnosis of generalized psoriasis.

DR. R. J. KELLY: The eruption on the face appeared several months after the eruption on the legs. Histologic examination of tissue taken on December 5 from an area just anterior to the right ear showed lupus erythematosus.

DR. SAMUEL M. KAUFMAN: The patient was presented at a conference at the Vanderbilt Clinic, and my diagnosis of his condition was that of lupus erythematosus of the scalp and face. Another opinion given at that time was that of lichen planus. The interesting feature in this case is that a second eruption is present, psoriasis involving both legs. It is rather difficult in some cases to differentiate between lupus erythematosus and psoriasis; however, my reason for diagnosing lupus erythematosus of the scalp is the character of the lesions, which show atrophy, alopecia and hyperkeratotic plugs.

DR. PAUL GROSS: Even the clinical picture of the lesions on the face suggests lupus erythematosus, since close inspection reveals patent follicles and small keratotic plugs. More important, I believe, are the medical aspects of this case, namely, the albuminuria and the outspoken coproporphyrinuria. Further study will have to establish the absence or presence of a systemic lupus erythematosus. The occurrence of lupus erythematosus and psoriasis in the same patient may have a common etiologic background.

NOTE.—The patient was hospitalized shortly after presentation, and a thorough medical work-up revealed hepatic damage due to chronic alcoholism and secondary anemia. There was no leukopenia. There was improvement of all the cutaneous lesions from intensive liver and yeast therapy.

Carotenemia. Pityriasis Rosea? Xanthomatosis. Presented by DR. F. PHILIP LOWENFISH.

W. G., a boy aged 3 years, is presented from Vanderbilt Clinic with lesions of the trunk, abdomen and neck of six weeks' duration.

Tawny colored oval lesions are seen on the front and back of the chest and abdomen, running along the lines of cleavage. The edges are slightly raised, and in some the centers have a cigaret-paper-like appearance. The knees, palms and soles are yellowish.

The patient is diabetic and has been taking 12 units of insulin a day for a year. He went into a coma a year ago, and the diagnosis of diabetes was made then.

The serum cholesterol content was 212 mg. per hundred cubic centimeters. The blood sugar amounted to 441 mg. per hundred cubic centimeters. There was a 2 plus reaction for carotene. Examination of the lesions on the back showed no fungi.

DISCUSSION

DR. MAURICE J. COSTELLO: Carotenemia has been described in association with diabetes mellitus (Pariente, A. C.; Present, C. H., and Ralli, E. P.: A Case of Carotenemia and Diabetes Mellitus, Am. J. M. Sc. **192**:365 [Sept.] 1936). I think that all of the cutaneous manifestations in this case are those of carotenemia associated with diabetes mellitus.

DR. PAUL GROSS: This case illustrates better than the preceding one the fact that two types of eruption may occur from a common cause. The appearance of the skin is characteristic of carotenemia, although the yellowish discoloration of the folds of the palms may be xanthomatous. The severe diabetes indicates profound disturbances involving the liver as well as the pancreas. This condition has resulted in the inability of the liver to hydrolyze carotene into vitamin A, and the disturbance of the cholesterol metabolism has resulted in xanthoma.

DR. FRANK C. COMBES: Would not xanthomatosis be expected to respond more promptly to insulin? One would expect that the cholesterol content of the blood would become normal after a short time, even before the blood sugar.

DR. E. WILLIAM ABRAMOWITZ: I do not think the condition is xanthoma at all. I have the impression that it is a pityriasis rosea in which the lesions have taken on the color of the carotenemia that is also present.

DR. F. PHILIP LOWENFISH: When I first saw the patient, about three weeks ago, I believed the condition to be pityriasis rosea. There was a large herald patch on the right side of the back; the other lesions were smaller, oval and discrete and were situated along the lines of cleavage running down around the chest. I noticed the yellow infiltration on the palms, soles and knees. Both carotenemia and xanthomatosis are to be considered.

Paraffinomas. Presented by DR. BEATRICE M. KESTEN.

M. B., a white woman aged 54, was born in the United States. In 1912 she consulted a beauty specialist because of depressions in her cheeks, above the collar bones and above the sternum. She received "injections" of a substance in these areas and was assured that paraffin had not been used. The depressions disappeared, and the patient had no trouble until June 1939, when she noted lumpy swellings.

On admission to Vanderbilt Clinic, on Sept. 10, 1939, the patient had massive, irregularly outlined swellings of the aforementioned areas. There was no inflammation. The surface was glossy and pale, with veins radiating outward symmetrically from the center of the face. On palpation the masses were firm and adherent, except for one in the right supraclavicular region. This one was excised, and histologic examination was made.

The specimen consisted of a mass of fairly firm tissue, acorn shaped, 3.5 by 2 by 1 cm., fixed in Bouin's fluid. On section a finely trabeculated cut surface

was seen. Sections revealed poorly encapsulated, dense fibrous tissue containing numerous collections of cystic vacuolations surrounded by many foreign body giant cells. These collections were separated by trabeculations of fairly dense fibrous tissue, and scattered lymphocytes were seen throughout. Along one side of the section there were bundles of striated muscle. There were also foamy cells in the fat. The histologic diagnosis was "foreign body in the lateral cervical region (paraffin)."

The mass in the center of the forehead received a total of 2,600 r of roentgen rays (100 kilovolts, screened with 3 mm. of aluminum) between Oct. 9, 1939 and Jan. 11, 1940, without perceptible improvement.

The patient noted that after the ingestion of salt, milk or egg these areas became more swollen. Elimination diets, epinephrine and ephedrine were tried. The swelling did not subside after administration of epinephrine, and ephedrine sulfate made the patient ill. In the course of the diets it was observed that pork, milk, fish and salt caused a definite edema in the swellings. After the injection of ammonium chloride for cystitis severe edema occurred.

A Case for Diagnosis (Lipogranulomatosis? Paraffinoma?). Presented by DR. J. GARDNER HOPKINS.

S. M. S., a white woman aged 34, a patient of Dr. J. K. Fisher, was born in Puerto Rico and has been in the United States for seven years. One sister died of tuberculosis.

The patient had painful swellings of both legs at the age of 8 years and could not walk for one year at that time. She has had bronchitis at times during the past ten years and takes cold easily. She has been pregnant twice, with twins at the first delivery about two years ago; the second delivery was two months ago, at which time she received injections of infundin (an aqueous solution of posterior pituitary) and ergonovine malleate, together with a blood transfusion. She received no other injections. (This report is from the hospital where the delivery took place.)

About three weeks ago, one month after delivery, pains developed in each arm from the elbow to the shoulder, first and more severe in the left arm. The pain was not aggravated by movement, and she did her housework. About one week later the arms began to swell and were warm in these painful areas. The pain was severe for two weeks, more so at night. She states that the arm felt as though it was tightly bound and the areas as though they were bruised. About one week ago similar painful areas appeared on the anterior portions of the thighs. She says that she feels "needles" in her hands at night.

Examination of the blood showed hemoglobin 80 per cent, red blood cells 4,300,000, white blood cells 4,700, polymorphonuclear leukocytes 45 per cent, lymphocytes 50 per cent, eosinophils 5 per cent, calcium 10.5 mg. per hundred cubic centimeters, phosphorus 4.2 mg. and Wassermann and Kline reactions negative. The urine gave an acid reaction and contained a trace of albumin. The basal metabolic rate was + 17 per cent. A roentgenogram of the chest revealed no recent parenchymal infiltration. A roentgenogram of the left arm showed some amorphous shadows of metallic density projected through the soft tissues, the nature of which was not clear.

Histologic examination showed no remarkable change in the epidermis. The corium was the site of a diffuse inflammation. There were perivascular foci of a mononuclear infiltration, a diffuse slight edema and a scattering of polymorphonuclear leukocytes. The blood vessels showed evidence of engorgement. The most profound changes were noted in the deep part of the corium and in the subcutaneous fat. Here there was evidence of a fibroblastic proliferation which had partly replaced the fat lobules. Large numbers of polymorphonuclear leukocytes were noted. There were also tubercle-like infiltrations with epithelioid cells. Some of these enclosed large clear spaces which looked like huge fat cells.

Partly calcified irregularly shaped hollow structures were surrounded by zones of hyalinized acellular connective tissue; this in turn was surrounded by a definite granulomatous infiltration. Sections stained with scarlet red showed evidence of smearing, but this stain seemed to bring out the presence of a lipoid-containing substance in the centers of the hyalinized nodules, the tuberculoid nature of the infiltration and the presence of calcification.

The histologic diagnosis was as follows: tuberculoid granuloma (paraffinoma?) and foreign body granuloma with calcinosis and cellulitis.

DISCUSSION OF PARAFFINOMAS

DR. J. GARDNER HOPKINS: There was one interesting point about the first case: the variations in the intensity of the swelling. That emphasizes what one sees under the microscope: The mass is due not to the paraffin itself but to the inflammatory reaction about it. Dr. Kesten acquired the patient after the plastic surgeons had "thrown up their hands." It has been interesting to observe that the degree of inflammatory swelling in this case can apparently be controlled to some extent by diet.

DR. HERMAN SHARLIT: Is there anything in the history to indicate what might have precipitated this reaction after twenty-five years of more or less benevolent symbiosis? Twenty-five years with no trouble is rather a long time.

DR. E. WILLIAM ABRAMOWITZ: I believe the condition in Dr. Hopkins' case is not a paraffinoma on account of the rather rapid onset after the injection of substances, two or three months. Usually paraffinomas appear years after the paraffin has been injected. I think the woman received injections of some substance that induced changes in the fatty subcutaneous tissue.

DR. JEROME K. FISHER (by invitation): It seems contradictory that the second patient was given so many injections of a posterior pituitary preparation. Normally they are given only a few times during delivery. I am also wondering whether the history is complete. I think the diagnosis is still questionable.

DR. BEATRICE M. KESTEN: As to Dr. Sharlit's question, I do not know what precipitated the condition. One reason I presented the case is to show the development and disappearance of these paraffinomas according to diet. After the ingestion of milk, salt and iodine the woman is unable to see, for then the paraffinomas reach their greatest proportions. After a genitourinary disturbance the patient was given ammonium chloride and had one of her worst attacks of swelling of the face.

Macular Atrophy (Anetoderma of Jadassohn). Presented by DR. GEORGE C. ANDREWS.

R. H. U., a woman aged 28, has spent all her life in Puerto Rico except for an occasional short visit to other countries. She was first observed in May 1939, with a generalized asymmetric eruption on the legs, thighs, buttocks, abdomen and face of eighteen months' duration. Recent examination reveals no change in the eruption except for the development of a few new lesions.

The condition is characterized by the development of round to oval, white, cicatricial areas, some of which are slightly depressed and others elevated with subcutaneous induration. There is no bladder-like distention of lesions, and none of them can be inverted. A few of the lesions on the abdomen which were treated with ultraviolet radiation show peripheral pigmentation. These spots persist unchanged; they do not increase in size beyond ⅛ to ¾ inches (0.3 to 2 cm.), nor do they disappear. There have been no subjective symptoms.

General physical examination by an internist showed no abnormalities except for soft teeth with many fillings and slight scoliosis. Large cryptic tonsils were removed one year ago. The blood pressure was 105 systolic and 90 diastolic.

Neurologic examination showed narrowing of the visual fields, loss of pharyngeal and corneal reflexes and slight sluggishness of the achilles and abdominal reflexes.

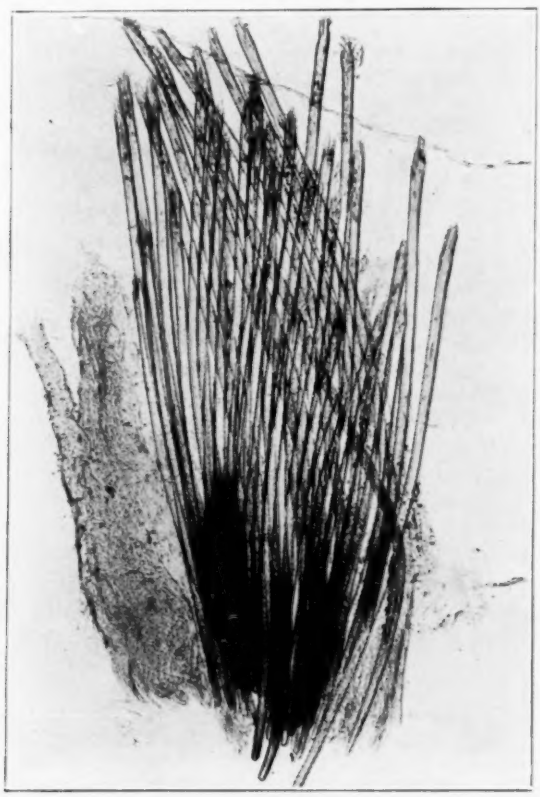
There is a past history of chronic sinusitis, frequent colds and hookworm infestation in childhood, but recent examinations of the stool have shown none of the parasites. One brother died at the age of 21 of pulmonary tuberculosis.

The Wassermann and Kahn reactions of the blood were negative. There was a strongly positive reaction to tuberculin in a 1 : 1,000,000 dilution. Roentgenograms of the chest were normal except for showing some calcification of the left hilus. The basal metabolic rate and the urine were normal, and the blood count was normal except for 9 per cent eosinophils.

Histologic examination by Dr. Gerald F. Machacek showed changes suggesting a localized scleroderma.

Trichostachis Spinosa. Presented by DR. GERALD F. MACHACEK.

R. F., a woman aged 46, came to the ophthalmologic department of Vanderbilt Clinic on Jan. 17, 1940 with chronic conjunctivitis. On February 7 she was referred to the dermatologic department for scaling of the scalp and macules and papules



Trichostachis spinosa.

of the face, which was diagnosed as seborrheic eczema. Treatment consisted of topical applications and roentgen ray and ultraviolet irradiation. After a peeling dose of ultraviolet rays was given herpex simplex developed on the lip. The condition improved but redness persisted. She was referred to Dr. Gross for

treatment of rosacea, and 2 mg. of riboflavin was administered, with improvement. While she was undergoing this treatment tiny black spots of a follicular nature were discovered which were slightly raised to the touch. Many were extracted and were found to consist of bundles of short hairs, rounded at the external ends and frayed at the ends remaining within the follicles.

MANHATTAN DERMATOLOGIC SOCIETY

J. FRANK FRASER, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Jan. 14, 1941

Argyria. Presented by DR. ISADORE ROSEN.

J. F., a girl aged 7 years, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 13, 1941 because of discoloration of the conjunctivas and of the skin of the nose.

The history revealed the frequent application of 10 per cent mild protein silver (argyrol) to the nose and eyes by the mother every time the patient had a cold. These instillations have taken place since the age of 1 year. Three years ago attention was called to this pigmentation by physicians, but no instructions were given as to the discontinuation of administration of the mild protein silver, which has been continued until the present.

The conjunctivas are of a peculiar slate color. Similar pigmentation is on the sides of the nose and on the hard palate.

DISCUSSION

DR. MAX SCHEER: Nothing can be done for this patient. I have tried Stillians' treatment without any result. Silver utensils turn black if not cleaned often, and I wonder what this black compound is chemically and whether patients who eat and drink out of such dishes could get argyria.

DR. GEORGE ANDREWS: I also tried Stillians' treatment thoroughly without success. However, at the last meeting of the American Academy of Dermatology and Syphilology, in Chicago, I saw a patient whom Dr. Stillians had treated with good results. The patient stated that she had received thousands of injections. Perhaps I did not persist sufficiently in my case to get satisfactory results. I have in mind another patient whom I treated with sodium thiosulfate intravenously about six years ago. That man was of dark slate color. He was in my office recently about some other matter and was not noticeably slate colored. I do not know whether the improvement was spontaneous or due to the treatment. He received two or three injections a week for about three or four months. He had no other treatment. I wonder if a patient's diet has anything to do with the intensity of argyria. I wonder if a lot of sulfur in the diet might make the condition worse.

DR. HERMAN SHARLIT: Histamine might be tried. It definitely increases the flow of lymph, and the particles of silver may be carried away from the surface so that they will not show. Histamine is good for black and blue marks.

DR. E. WILLIAM ABRAMOWITZ: In the excellent monograph by Hill and Pillsbury (Argyria, The Pharmacology of Silver, Baltimore, Williams and Wilkins Company, 1939) it is stated that there is no agreement on the type of silver compound present in the skin in argyria. Various treatments have been used for argyria, but none of them have been efficacious, including sodium thiosulfate, potassium iodide and the reducing solution that Stillians uses. The reducing solution is also used in a diagnostic test. I think that sodium thiosulfate has

very little effect, if any, on any metal retention in the body; in fact, it has been shown that it might act contrariwise. In view of the fact that in some cases of argyria the pigmentation fades although no treatment is given, the possibility must be considered that some of the pigmentation may be removed by the natural forces of the body.

DR. WILBERT SACHS: I have a patient who received two hundred injections of silver arsphenamine over a period of five or six years. When I saw her the mucous membrane of the pharynx and of the palate was entirely black. I gave her injections of sodium thiosulfate twice a week for several months. There was no change in the pigmentation.

DR. DAVID BLOOM: It is of interest to note that the attention of the mother was called to the pigmentation of her child several years ago by physicians, but none of them warned her about the use of mild protein silver. She, therefore, continued using it until two weeks ago.

DR. HOWARD FOX: Has any one present ever observed a case of argyria in which the pigmentation disappeared spontaneously?

DR. FRED WISE: In 4 cases of argyria that I have observed over a period of fifteen years the discoloration has not shown any tendency to fade.

DR. MAURICE J. COSTELLO: In recent years a number of cases of argyria have been presented at meetings of dermatologic societies. In nearly every instance the offending agent was mild protein silver which had been self administered daily for months, and in nearly every case it was administered by instillation in the eyes, nose and throat. The majority of the patients stated that they bought this medicament freely over the counter in the drug store and that there was no warning on the label to indicate that the prolonged use of the substance might cause argyria. Laws should be enacted to protect the public from this disfiguring hyperpigmentation which follows the indiscriminate use of this drug.

Naevus Unilateralis Comedonicus. Presented by DR. GEORGE M. LEWIS.

C. L., a boy aged 10 years, is presented from the New York Hospital, with a lesion on the left side of his forehead which has been present since birth. Some increase in size has been noted, probably in direct proportion to an increase in age. There has been no treatment prior to presentation.

The lesion consists of a raised, reddened plaque. Throughout are many comedo-like dots. One of these was expressed and was seen to be a comedo. Further examination of the patient shows no abnormalities.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I should like to simplify the diagnosis and call the condition a linear nevus.

DR. GEORGE M. LEWIS: There are many types of linear nevus. The presence of comedos seems to make the condition in this case a clearcut example of comedo nevus, true examples of which are not common.

Hemorrhage, Necrosis and Atrophy of the Skin in a Patient with Endocrine Disturbance. Presented by DR. SAMUEL M. PECK.

A white woman aged 46, born in United States, stated that as near as she could tell, the eruption began about twelve years ago with dryness of the skin of both arms and legs, accompanied by itching. Two years ago there was an exacerbation of all signs and symptoms accompanied by loss of hair of the eyebrows and of the scalp. The menstrual periods were irregular. Physical examination showed no abnormalities. The patient stated that previous to the onset of this condition (about three years ago) she had a great deal of hair on the arms and legs as well as in the axillas. The hair on her scalp too was thick.

The scalp is covered with diffuse fine scales, and the hair is rather thin and dry. The eyebrows are scanty and are practically gone along the outer half.

The eyelashes are well maintained. Axillary hair is missing on both sides, and the genital hair is scant. There is no hair on other portions of the body. The skin of the face is edematous and definitely thickened, so that the eyes appear sunken. There are accentuation of the cutaneous folds and fine scaling; the color of the skin is faintly erythematous, and the cheeks show fine telangiectasia. The mucosa of the mouth is normal. Scattered over the anterior and posterior surfaces of the trunk there are minute hemorrhages and small superficial ulceration. The skin of the chest and of the back, as well as that of the arms and of the legs, is wrinkled, atrophic, bluish red, thickened and dry. The epidermis seems to be too large for the underlying structures, so that it seems to fit loosely, and the lines of the skin are exaggerated. The hemorrhagic areas are irregular in shape, varying from 1 to 3 cm. in diameter. Such hemorrhagic areas often go on to superficial ulcerations, which later form dry crusts. The healing of such places is rather rapid. On the legs, however, is a different situation. The skin there is somewhat suggestive of acrodermatitis chronica atrophicans in that the subcutaneous vessels are clearly visible, owing to the disappearance of fat. Hemorrhages are also seen on the legs; ulcerations are seen around the calf, and there they last for months. Due to the edema of the skin the patient's movements are limited. The skin of the palms and of the soles is also dry. The nails are not much affected. Ulcerations are also seen around the ankles.

A complete examination of the blood and of the marrow obtained on sternal puncture showed no abnormalities except moderate eosinophilia. The reaction to a Kahn test was negative, and the blood sugar content was normal. The total cholesterol content was 345 mg. per hundred cubic centimeters, with 230 mg. of cholesterol esters. The result of a dextrose tolerance test was normal. The basal metabolic rate was + 21 per cent. The reaction to a venom test was positive, indicating a generalized capillary fragility. A gland was removed from the right axilla, and histologic examination showed chronic and acute hyperplasia with striking eosinophilia. A biopsy of tissue from the right thigh showed substantial hyperkeratosis, acanthosis and edema of the epidermal cells, both intercellular and intracellular. Follicular hyperkeratosis was present. There was considerable edema and infiltration throughout the layers of the cutis. The infiltration consisted of dense accumulations of lymphocytes and large mononuclear cells around and between the vessels. The histologic changes were suggestive of an early stage of lymphoblastoma or a toxic condition of long standing.

Dermatitis Venenata Due to a Wooden Necklace. Presented by DR. DAVID BLOOM.

F. M., a woman aged 22, a private patient, consulted on Dec. 31, 1940, for a mildly pruritic eruption on her neck of one week's duration. On examination there was on the posterior and lateral aspects of the neck a ring 3 inches (7.5 cm.) wide which was erythematous and scaly. The anterior portion of the neck was free from the eruption.

Questioning of the patient pointed to three possible causative agents: a red woolen sweater, a green corduroy dress and a wooden necklace. Patch tests were made with the sweater, with the dress material and with one of the wooden pieces of the necklace. Examination after twenty-four hours showed a positive reaction, consisting of erythema and vesiculation, to only the wooden piece. The patient procured the necklace in the last week of November 1940 and has worn it since then about six times. On December 23, a few hours prior to the development of the eruption, the patient was given a permanent wave, at which time a sheet was tightened around her neck pressing the necklace close to the skin.

NOTE.—After the presentation another patch test was made with a wooden piece of the necklace from which the lacquer was removed. A positive reaction was obtained after twenty-four hours, which indicates that the patient's skin was sensitive to the wood.

DISCUSSION

DR. FRED WISE: I regard the eruption as an early phase of dermatitis atrophicans.

DR. E. WILLIAM ABRAMOWITZ. I suggest that the patient presents an atrophoderma associated with a thyroid disturbance.

DR. DAVID BLOOM: If I were to disregard the presence of hemorrhages in the skin, I should consider this case as one of generalized atrophy of the skin analogous to acrodermatitis chronica atrophicans, which involves the extremities only.

DR. SAMUEL M. PECK: One cannot obtain a clearcut picture of the course of some of the patient's lesions unless she is observed for a few weeks or so. The origin and course of an ulcerated lesion can then be really seen. Her blood vessels cannot be seen because of considerable edema. The atrophy is not like that seen in acrodermatitis. It is interesting to note that on her chest and abdomen there are areas of skin which seem practically normal. The cause of the hemorrhagic lesions may be explained by the fact that with the loss of elastic tissue the fragile capillaries lack support and with any increase in pressure rupture. This would not explain the necrosis, however. It seems to me that a process such as thrombosis of an arteriole with the formation of an infarct is a much more plausible explanation. It will be of interest to see if scleroderma-like changes develop in the future.

Macular Atrophy (Anetoderma of Jadassohn) in a Ten Year Old Boy. Presented by DR. GEORGE M. LEWIS.

A. R., a boy aged 10 years, is presented from the New York Hospital with multiple lesions on the trunk. The condition was first noticed three years ago. New lesions have continued to form. There are no subjective symptoms. No inflammation has been noted at any time.

Inspection shows two types of lesions. The more numerous are flat or depressed, light brown, superficial and atrophic. There are a few lesions which show bulging or semiherniation. This is confirmed on palpation, the center being depressed and soft and the margins firm. Many lentigines are noted scattered over the trunk.

The histologic section from a bulging lesion showed a flattened epidermis overlying a corium which showed keloid-like thickening. The rete pegs had disappeared entirely, and there was moderate pigmentation of the basal cell layer. There was a slight perivascular infiltration in the corium by lymphocytes and plasma cells. Histologic examination of a specimen from a flat lesion showed elastic tissue fragmentation and destruction.

Urticaria Pigmentosa and Lichen Planus of Simultaneous Onset. Presented by DR. GEORGE C. ANDREWS.

E. N. R., a Mexican aged 37, was presented before the New York Dermatological Society on Jan. 28, 1941 (ARCH. DERMAT. & SYPH., to be published).

DISCUSSION

DR. FRED WISE: My impression is that the patient has two different diseases.

DR. MAX SCHEER: The lesions of urticaria pigmentosa which were macular became definitely elevated on slapping, which I am not aware can happen in lichen planus. I therefore accept the diagnosis as presented.

DR. ISADORE ROSEN: I agree with the diagnosis as presented. I never saw generalized lichen planus with such a uniformity in color and appearance. The hypertrophic lesions on the wrist have entirely different clinical features from the eruption elsewhere. The patient also presents definite lichen planus of the buccal mucosa.

DR. HOWARD FOX: I think this combination of two entirely separate diseases, one of which is rare, is most unusual. Clinically, the lesions on the wrists and in the mouth are typical of lichen planus and those on the body are typical of the adult type of urticaria pigmentosa.

DR. PAUL E. BECHET: I agree with the diagnosis as presented. All the cardinal clinical symptoms of both dermatoses are clearly and definitely depicted. I have never been able to understand why the simultaneous occurrence of two different cutaneous diseases in the same patient should cause such hesitancy on the part of the average dermatologist in making a diagnosis of two diseases.

DR. DAVID BLOOM: Until more information is available in regard to the pathogenesis of lichen planus and of urticaria pigmentosa, their association in the same patient must be considered a coincidence. But because of present ignorance as to their causation the recording of this association must be considered important.

DR. E. WILLIAM ABRAMOWITZ: I agree with the presenter that this man has urticaria pigmentosa as well as lichen planus.

DR. GEORGE ANDREWS: The adult type of urticaria pigmentosa seems to have a striking and typical appearance. The lesions are so uniform and the urtication is so characteristic that no doubt can be raised about the accuracy of this diagnosis. There is also definite annular lichen planus of the left wrist, which no one disputes.

Acrodermatitis Continua (Hallopeau). Presented by DR. GEORGE M. LEWIS.

F. G., a white man aged 29, had lesions of the fingers which first developed three and a half months ago. He has been under treatment for the past two months. New pustular lesions were noted to form during this period. There was no history of injury previous to the onset. The paronychial tissue was primarily affected with pustular, crusted, edematous lesions. The thumb, index finger and middle finger of the right hand were chiefly involved. Pustules were also noted on the left hand. The nails of the involved fingers showed varying degrees of dystrophic changes.

The mycologic examination (direct mount and culture) gave negative results. The trichophytin test elicited a 2 plus reaction after forty-eight hours and after one week. The Wassermann reaction was negative. Treatment consisted of applications of a 1 per cent aqueous solution of gentian violet and potassium permanganate soaks.

DISCUSSION

DR. SAMUEL M. PECK: I do not agree with the diagnosis as presented. If there were more lesions on the feet, I should be inclined to consider the diagnosis of so-called recurrent pustular eruption of the hands and feet. Pustular psoriasis and epidermophytosis must also be considered.

DR. MAX SCHEER: The presence of some "small lakes" of pus and the pustules on the palms and lesions originating from various parts of the fingers makes me think that the condition is a pustular bacterid, such as Andrews described some years ago.

DR. FRED WISE: In my opinion, Hallopeau's acrodermatitis perstans is a definite and distinct disease entity, the course and symptoms of which do not correspond to the clinical manifestations presented by this patient in any essential details.

DR. GEORGE ANDREWS: I recommend that sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) be tried.

DR. ISADORE ROSEN: I am of the opinion that the changes of the nail which the patient presents are due to some constitutional disturbance rather than to acrodermatitis perstans of Hallopeau. The latter is usually an inflammatory vesiculopustular disease producing lesions which are considerably undermined and destructive. These features are not present in this case.

DR. E. WILLIAM ABRAMOWITZ: Dr. Andrews' suggestion of administering sulfathiazole is a good one. I observed several cases of a pustular eruption of the hand with paronychia, in which cultures showed hemolytic streptococci. The response to sulfanilamide was astonishing. However, I think that a 5 per cent ammoniated mercury ointment applied to the hands will cause a cure.

DR. DAVID BLOOM: Has a repeated bacteriologic examination of the pus from the pustules been carried out?

DR. GEORGE M. LEWIS: I am not surprised that there is some difference of opinion as to the diagnosis. The patient has improved considerably; so many of the features present when he first came to the hospital are now not evident. When I first examined the patient, three fingers were affected, and in spite of treatment further spreading occurred. At first there were bulbous paronychial swellings with undermining of the edges and lakes of pus so characteristic of this disease. There were considerable pain and tenderness. I do not believe the further spread of the condition is against a diagnosis of acrodermatitis; in other instances this has been noted. The bacteriologic and mycologic studies gave negative results. Furthermore, on clinical grounds, dermatophytosis, pustular psoriasis and paronychia could be distinguished and eliminated from consideration. The urine did not contain demonstrable sugar, and there was no history of ingestion of any drug. For these reasons I still favor the diagnosis under which the patient was presented.

Cheilitis (Pyoderma or Ariboflavinosis). Presented by DR. E. WILLIAM ABRAMOWITZ.

S. G., a woman aged 19, was well until about three and a half years ago. At that time diarrhea suddenly developed, and she had fifteen or twenty bowel movements each day. There was no associated elevation of temperature. This acute attack was controlled by dietary and medical therapy. She was fairly comfortable except for occasional attacks throughout that year. Two and a half years ago the attacks changed; the stools included blood and mucus, and she had abdominal cramps. She was admitted to the Brooklyn Jewish Hospital, where proctoscopic examination revealed colitis and the aspirated fluid, which was cultured, revealed Salmonella. She was treated with a salmonella vaccine along with a high protein, high caloric and high vitamin bland diet. On this regimen many of her symptoms were checked. For the remainder of that year she had one to three stools per day. Despite this improvement spongy gums and sores on her buccal mucosa developed.

Six months ago her eyes became reddened, and there was lacrimation along with a mucopurulent discharge. Three months ago she had several crusted lesions on her scalp, with similar crusts, yellow scales and vegetations on her lips. A swelling appeared above her left ear; crusting along the sides of the nose, as well as in her left nostril, and a whitlow on her left index finger were noted. At this time she visited the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. Examination did not show Monilia. Smears of material taken from her mouth showed Vincent's organisms. At present—and for the greater part of the past year—she has some abdominal cramps, but not more than three or four daily stools, which are loose but not watery or bloody.

The blood count showed red blood cells 3,520,000, white blood cells 6,800, polymorphonuclear leukocytes 41 per cent, lymphocytes 39 per cent, eosinophils 13 per cent and mononuclear leukocytes 7 per cent. Examination of the blood for vitamins showed carotenoids 0.12 mg., vitamin B_6 0.02 mg. and vitamin C 518 mg. per hundred cubic centimeters in five hours. The Wassermann reaction was negative. The urine was normal but showed minimal quantities of riboflavin. The stool culture showed hemolytic and nonhemolytic lactic acid bacilli, along with 1 per cent nonhemolytic streptococci. Analysis of the gastric contents showed normal results. The basal metabolic rate was —6 per cent. Roentgeno-

grams of the gastrointestinal tract suggested either dysenteric infection or ulcerative colitis.

The patient was admitted to the hospital. Her temperature curve was normal except for two occasions when there was a moderate elevation to 100 to 101 F. She was given a high protein, low residue diet; 5 mg. of riboflavin four times per day; 100 mg. of nicotinic acid amide three times a day; 2 capsules daily of a mixture of vitamins (hepicelrin) containing in each capsule 10,000 U. S. P. units of vitamin A, 200 international units of vitamin B_1 (0.6 mg. of thiamine hydrochloride), 40 Sherman-Bourquin units of vitamin G (B_2) (100 micrograms of riboflavin), 500 international units of vitamin C (25 mg. of ascorbic acid) and 1,000 U. S. P. units of vitamin D; 3 Gm. of ryzamin-B (a rice polishing concentrate containing 80 international units of vitamin B_1 per gram) three times a day by mouth; 20 mg. of thiamine hydrochloride per day, and 3 cc. of campolon (an injectable liver extract), 3 cc. intramuscularly per day. There was some improvement in the lesions on the skin and lips during her short stay in the hospital.

A proctoscopic examination showed ulcerated areas which were pale pink and thickened. The ulcers were in groups, were shallow and measured about 3 mm. in diameter. The impression was that, in view of the cellular exudate, there probably were innumerable ulcerated areas higher up in the intestine beyond the area visualized.

DISCUSSION

Dr. George M. Lewis: There is a history of ingestion of iodized table salt. This may be a significant item, since ioderma could explain at least part of the eruption, namely, the papillomatous, crusted lesions of the lip and scalp. Determinations of the blood level of iodides might be helpful.

Dr. Samuel M. Peck: Cutaneous manifestations of true vitamin A deficiency respond more readily to treatment with the vitamin in question. This is not evident in this patient. The fat-soluble vitamins seem to cause more fundamental changes in the skin when they are deficient. Also they act much more slowly in affecting changes in the skin.

Dr. Isadore Rosen: I saw this patient on admission to the clinic and was able to study the condition carefully. There has been a substantial improvement in the general characteristics of the eruption. When first seen the lesions on the outer surfaces of the lips were vegetating, while the inner surfaces were studded with small glistening pinhead-sized tubercle-like lesions, suggesting tuberculosis of the mucous membrane. At present there is no evidence of the latter. I am of the opinion that there is a direct connection between the colitis and lesions on the skin and mucous membranes.

Dr. Maurice J. Costello: I think the fact that the tongue is normal is against the diagnosis of vitamin B deficiency. Usually patients with this condition have a glazed smooth tongue. This is true especially of the patients observed in the wards at Bellevue Hospital in the spring and summer suffering from alcoholic pseudopellagra.

Dr. David Bloom: I agree with Dr. Rosen that the patient has improved since her stay in the hospital. I think that the suggestion of Dr. Lewis should be considered, that an examination for iodides be made.

Dr. E. William Abramowitz: While the patient was at the hospital she received vitamins by injection, and since that time there has been some improvement. The histologic examination showed an almost pure plasma cell infiltration, and that is not the picture altogether of a bromoderma or iododerma. However, it may be that iodides have aggravated her eruption.

Note.—A subsequent investigation disclosed that no iodized salt had been used for over a year.

Lichen Planus of the Mucous Membranes in Two Sisters.—Presented by Dr. David Bloom.

Case 1.—C. S., a woman aged 60, came to the clinic of Sydenham Hospital on Jan. 8, 1941 with an eruption of the mucous membranes of the mouth. Two months previously she noticed slight soreness in her mouth and thus discovered the eruption. A physician has treated her since then with applications of toughened silver nitrate to the lesions at intervals of two weeks. Seven months ago the patient had her teeth extracted, and one month after wearing new dentures she noticed soreness on the left lateral aspect of the tongue, which made her discontinue wearing the denture.

The patient has had pruritis of the vulva and of the groins for the past twenty-five years. On examination these areas present lichenification, erythema and several darkly pigmented, raised, pea-sized lesions. The past history was otherwise normal.

On examination the mucous membranes of the cheeks at the level of the lateral teeth show milky white, reticulated, irregularly shaped plaques, which extend anteriorly toward the mucous membrane of the lower lip. The plaques are slightly excoriated, probably owing to the application of the toughened silver nitrate. The tongue shows, on the left lateral aspect and on the dorsum of the right side, pea-sized whitish plaques which seem to be somewhat depressed.

The Wassermann reaction of the blood was negative. The microscopic examination of the lesion of the groin by Dr. Wilbert Sachs showed the structure of lichen planus.

Case 2.—A. D., a woman aged 55, the sister of C. S. (case 1), noticed soreness in the mouth one month ago. The past history of the patient showed nothing of significance except that an abdominal tumor was removed five years ago. The two sisters live together.

On examination the mucous membranes of the cheeks show at the level of the teeth an irregularly shaped plaque of milky white reticulation. On the vermilion border of the lower lip there are a few scaly papules and whitish flat reticulated lesions.

The Wassermann reaction of the blood was negative. Microscopic examination of the lesion on the left cheek confirmed the diagnosis of lichen planus.

DISCUSSION

Dr. Max Scheer: I can report cases of lichen planus in three brothers, two living in Cleveland—and not living together because they were married—and the third living in New York. Lichen planus developed in one at the age of 25 years, in another at 20 years and in the other much later. Also the son of the eldest brother had extensive buccal lichen planus. The three brothers happen to be my father and two uncles, and the son with this condition is my youngest brother.

Dr. Paul E. Bechet: Despite the fact that lichen planus has been occasionally reported in two or more members of an immediate family, I believe it is too rare an occurrence to assume etiologic significance. I should be more inclined to ascribe it to coincidence.

Dr. George Andrews: I have under treatment a father and son who have typical generalized lichen planus.

Dr. David Bloom: Goodman and Sulzberger in 1937 (Arch. Dermat. & Syph. **35**:1139 [June] 1937) reported a case of conjugal lichen planus and mentioned Spitzer, who in 1924 collected reports on 46 instances of familial lichen planus, in 7 of which the condition was conjugal. Up to 1937 10 additional reports of familial occurrence appeared, in 2 of which the patients were husband and wife. I believe that familial occurrence is not as infrequent as it seems. This indicates that lichen planus may be infectious. The fact, however, that in a number of cases lichen planus was reported in close relatives not living together may prove that there is also certain hereditary predisposition present.

Nevus Pigmentosus of the Tongue.—Presented by DR. DAVID BLOOM.

B. T., a Negress aged 32, has had an eruption on her tongue since birth. The dorsum of the anterior aspect of the tongue near the tip shows a transverse plaque consisting of discrete dark brown puncta, which apparently coincide with the tips of the papullae.

The patient has late latent syphilis, for which she is being treated with a bismuth compound arsphenamine.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I think that this pigmentation is of a nevoid nature. There are some members of the Negro race who have blue gums. I think that this patient has blue gums, with pigmentation of the tongue not due to bismuth.

DR. HERMAN SHARLIT: It has been my impression that pigmentation of the mucous membranes is universal in Negroes. Some have more and others less. The condition in this case is just an unusual pigmentation in a Negro.

DR. SAMUEL M. PECK: Dr. Becker in his exhaustive article on pigmentation of mucous membranes gives all the information needed (Becker, S. W.: Melanin Pigmentation, ARCH. DERMAT. & SYPH. **16**:259 [Sept.] 1927).

DR. DAVID BLOOM: I well remember the case of bismuth pigmentation of the tongue which Dr. Costello presented last year. At that time I mentioned that I had observed 2 or 3 cases of this kind. Bismuth pigmentation of the tongue, although also punctate, differs from the condition in the case just presented in that it is bluish black; in this case the macules are brownish. When the patient first came to the clinic no pigmentation of the gums was seen, but it is present now and is probably due to the bismuth compound administered. The remark that any pigmentation in Negroes is a nevus is not correct. Pigmentation in Negroes is common and is inherited like their black skin, but the term nevus does not apply to it. One rarely sees this type of lesion in Negroes.

Acarophobia and Neurotic Excoriations with Unusually Extensive Scarring. Presented by DR. PAUL E. BECHET.

J. S., a man aged 51, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for the relief of a severe dermatosis which had been present for six years. It began as an inflammatory itchy dermatitis on the upper and inner surfaces of the thighs. A diagnosis of scabies was made at the time, and there was complete healing after the use of a salve for two weeks. Several months later two "scabs" about 2 cm. in diameter developed on either side of the scalp anteriorly, just within the hair line. Each "spot" would "bite just as if an insect were there" and was so annoying that the patient would attempt to scoop it out with his nails, leaving a distinct hole, which was soon crusted. The lesions soon spread to the arms, trunk and legs. The patient states that the condition feels at first "like insects creeping," and then this sensation is followed by a severe niplike bite. He says he often sees insects with threads in front of his eyes. He presents, among other evidences of a disturbed psyche, loss of the sense of taste and absence of pharyngeal reflex. The conjunctival and palatal reflexes are normal.

On inspection he presents superficial and deep scars, pigmented patches and freshly excoriated lesions mostly on the anterior surface of the body, easily accessible to his nails. On the nose there are two bean-sized deeply excoriated ulcers, so deep that one almost resembles a rodent ulcer. Many large lesions in all stages of evolution are observed on the scalp. The oldest lesions show severe scarring and total alopecia. Parallel linear lesions up to 2 inches (5 cm.) in length are observed on both sides of his neck.

Examination of the urine and of the blood, both chemically and microscopically, demonstrated no abnormality. Histologic examination showed nothing of significance.

Amyloidosis Cutis (Localized). Presented by Dr. George M. Lewis.

G. C., an Italian aged 63, is presented from the New York Hospital. An eruption first developed two years ago and has gradually increased in extent. There has been considerable pruritus. No treatment has been undertaken. The eruption is confined to the legs, below the knees. The individual lesions are small, rounded, shiny, hard papules of reddish brown. On palpation the lesions are firm to shotty. Many are closely set, tending to be confluent, and others are discrete. There are some lesions in linear distribution.

A physical examination showed no abnormalities except a moderate degree of hypertension (blood pressure, 172 systolic and 104 diastolic). The Wassermann reaction was negative. There was no personal or family history of syphilis or of tuberculosis. The reaction to a congo red test indicated amyloidosis. The histologic sections showed a thickened acanthotic epidermis with hyperkeratosis and a few patches of parakeratosis. There was a decided pigmentation of the basal cell layer. At the midpoint of the section the epidermis was atrophic, and directly beneath it was a discrete rather homogeneous, relatively acellular mass of connective tissue which resembled an organized thrombus. Directly beneath this and all through the superficial layer of the corium there was a heavy perivascular infiltration of lymphocytes, eosinophils and a few neutrophils. Examination of the tissue immediately after staining with methyl violet showed a large portion of the homogeneous connective tissue beneath the epidermis to take the purple color which is indicative of the presence of amyloid. There were likewise numerous streaks of amyloid scattered beneath the epidermis elsewhere.

CHICAGO DERMATOLOGICAL SOCIETY

Dr. Herbert Rattner, *President*

Dr. Michael H. Ebert, *Secretary*

Jan. 15, 1941

A Case for Diagnosis. Presented by Dr. Theodore Cornbleet and Dr. Alfred B. Falk (by invitation).

F. B., a white woman aged 45, states that two months ago she noticed for the first time a thickening of the skin of the small toe of her left foot, which was followed by a similar condition on the small toes of the right foot and, two weeks ago, by thickening of the skin of the right palm.

The patient has had six pregnancies, the second and third resulting in spontaneous abortions at five months. She has three children living and well. Eight years ago she had high blood pressure and heart trouble and was treated medically for three years. During the past five years she has been feeling well. There is no history of the ingestion of heavy metals or drugs of any kind in the past few years.

Examination reveals thickening and fissuring of the skin of the small toes bilaterally and of the right palm. The base of the lesions is somewhat red and vascular.

The urine showed a slight reaction for albumin. Serologic reactions for syphilis were negative. The results of chemical examination of the blood and the blood counts were normal. Examination of scrapings revealed no fungi. Histologic examination of the lesion on the left toe showed hyperkeratosis.

DISCUSSION

Dr. Udo Wile, Ann Arbor, Mich.: I have seen blenorrhagic keratosis start this way, but I hesitate to make this diagnosis with the condition in so early a

stage. Some hyperkeratotic and pustular lesions suggest that as a remote possibility.

DR. CLARK W. FINNERUD: I have observed 2 or 3 conditions almost identical with this one in the past two or three years, each in a woman of this age or older. I consider this condition a form of acquired keratosis which comes on about the time of the climacteric or later.

DR. H. J. PARKHURST, Toledo, Ohio: I agree with Dr. Finnerud.

DR. OTTO H. FOERSTER, Milwaukee: The condition may well belong to the Haxthausen type of menopausal dermatosis. In this patient the lesions are localized on the toes instead of being more diffuse, but this can possibly be an earlier stage than is customarily seen.

DR. JAMES H. MITCHELL: The Haxthausen type of keratosis is frequently discussed. I wonder whether it would fit in with a male climacteric. Whether or not men have a climacteric, they do have this type of keratosis. I have seen it as frequently in males as in females.

DR. THEODORE CORNBLEET: I considered angiokeratoma in the differential diagnosis, because the keratoses have a reddish cast. Unfortunately, the biopsy specimen was not taken deeply enough and does not show whether or not the lesions are angiokeratomas. There is no evidence in the history incriminating arsenic. No fungi are visible in the keratotic material on direct examination.

I entertained the thought of keratoderma climactericum. One should note, however, that this woman is still menstruating regularly. Of course, it is probable that cutaneous changes like this can occur or begin before the menses stop and still be included in the phenomena of the climacterium.

Sarcoid. Presented by DR. MICHAEL H. EBERT and DR. A. H. SLEPYAN (by invitation).

A woman aged 40 states that the lesion on the nose began about one year ago with tenderness and discoloration. She received hot applications and later several roentgen ray treatments. The lesion grew slowly. At present there is a violaceous plaque, 1.5 cm. in diameter, on the tip of the nose, extending from the middle over to the right ala nasi. The lesion is slightly raised and on diascopic pressure does not disappear but leaves a yellowish brown discoloration. There is slight involvement of the mucous membrane of the anterior vestibule of the nose. There are no other changes in the skin or any palpable lymph glands. There is no evidence of enlargement of the bones of the fingers. The microscopic picture was compatible with sarcoid.

DISCUSSION

DR. CHARLES C. TOMLINSON (by invitation), Omaha: I agree with the diagnosis of sarcoid clinically. I feel that the lesion is at least of a tuberculoid type.

DR. JAMES R. DRIVER, Cleveland: I agree with the diagnosis.

DR. F. W. LYNCH, St. Paul: I think that the clinical and histologic evidence is in favor of the diagnosis as presented. The large number of patients being presented with the diagnosis of sarcoid at all dermatologic meetings is evidence of the increasing general interest in the disease.

DR. UDO J. WILE, Ann Arbor, Mich.: I think it is worth while calling attention to the fact that the site of this lesion is the site of election for late syphilids in women. I think a diagnosis of a late syphilid would be almost as tenable as a diagnosis of tuberculosis or sarcoid, without histologic examination.

DR. JAMES H. MITCHELL: I wonder whether the condition might be a low grade streptococcic infection.

DR. HENRY E. MICHELSON, Minneapolis: I should like to make a warning remark, namely, that one should not make a diagnosis of sarcoid from the cutaneous observations alone. The lungs and bones should be examined, and, if

possible, a biopsy of the tonsil should be made in every case before a decision is made. One must keep in mind that the subject of sarcoid is by no means a settled one and that many facts are yet to be learned about this strange disease.

DR. MICHAEL H. EBERT: Originally this case was of interest to me because I felt that probably as a result of repeated infections in the anterior vestibule there was a continued eruption present in the area. However, the sarcoid-like structure histologically, to my mind, and also the history rule this out. Syphilis must be considered. This histologic structure is possible in a syphilitic lesion, but I should expect the cutaneous lesion to clear in the center and spread peripherally, although that does not always happen. The patient should have a therapeutic test with antisyphilitic drugs.

I have presented a few patients with Besnier-Boeck-Schaumann disease before this society. I realize that the disease involves many symptoms. I always have roentgenograms of the lungs and small bones taken and an examination of the nasopharynx made. I still feel that there is a disease known as localized sarcoid of a discoid or annular type even when it is not possible to find changes in these other organs, at least with the examinations at our command. I agree with Dr. Michelson that one should make all these examinations, even if the results appear to be negative, before a clinical and histologic diagnosis of sarcoid is given in this case.

DR. CLARK W. FINNERUD: In line with what Dr. Michelson and Dr. Ebert said about the localized type, one should recognize that the same histologic and clinical picture is produced rather definitely by micro-organisms other than the tubercle bacillus.

DR. MICHAEL H. EBERT: As a matter of fact, it is not known that Besnier-Boeck-Schaumann disease is caused by the tubercle bacillus.

Dermatitis Herpetiformis. Presented by DR. EDWARD A. OLIVER and DR. S. J. ZAKON (by invitation).

B. W., a white woman aged 70, came to the clinic of the Northwestern University Medical School on Nov. 20, 1937 with complaints of severe arthritic pains in the legs and arms. At that time she was found to suffer from hypertrophic arthritis, hypertensive cardiovascular disease, with a blood pressure reading of 205 systolic and 110 diastolic, and moderate obesity (weight 176 pounds [80 Kg.]).

The Wassermann and Kahn reactions of the blood were negative. The urine showed a 1 plus reaction for albumin and a few granular casts.

Examination of the blood showed 10,000 leukocytes, with 51 per cent segmented neutrophils, 15 per cent band cells, 5 per cent eosinophils, 20 per cent lymphocytes and 9 per cent monocytes. The basal metabolic rate was + 1.5 per cent. A roentgenogram showed decalcification of all bones. The sacroiliac joints showed mild arthritic changes.

She improved on diet and physical therapy management.

She returned to the clinic in June 1940, complaining of an eruption of six months' duration, consisting of vesicles, bullae, erosions and erythematous scaly patches of various configurations. The lesions were located on the face, arm, legs and abdomen, in the sacral area and over the scapulas. She complained of intense itching of such severity as to interfere greatly with sleep. A history of ingestion of drugs of any kind could not be elicited.

At this time urinalysis showed a 1 plus reaction for indican and a 1 plus reaction for albumin. Chemical examination of the blood showed: 37.7 mg. of nonprotein nitrogen, 3.53 mg. of uric acid, 1.45 mg. of creatinine and 122 mg. of sugar per hundred cubic centimeters. Further examination revealed 13 Gm. of hemoglobin per hundred cubic centimeters, 4,360,000 erythrocytes and 4,500 leukocytes, with a differential count of 49.5 per cent polymorphonuclear leukocytes, 2 per cent band cells, 1 per cent basophils, 33 per cent lymphocytes, 7 per cent monocytes, 5.5 per cent segmented forms and 2 per cent eosinophils.

Histologic examination on Jan. 2, 1941 showed edema of the corium, perivascular infiltration and intracellular and intercellular edema of the epidermis with vesicle formation.

At present a few of the lesions, especially those that are located on the shoulder and forearm, are purplish, angular and lichenoid.

DISCUSSION

DR. S. J. ZAKON (by invitation): Two months ago the patient had two lesions that were lichenoid in nature, and we thought of lichen planus plaques. She does not have them today.

DR. EDWARD A. OLIVER: We saw this patient about a month ago when the eruption was at its peak. In the supracapsular region she showed definite lichenoid angular shiny papules. There was some discussion when we examined her as to whether the condition might not be bullous lichen planus. Seeing her again today, I am certain that it is frank dermatitis herpetiformis.

DR. MICHAEL H. EBERT: I noticed that the patient had a whitish ring on the tongue. On being questioned she said that at the time of the exacerbation of the condition the tongue was rather sore. I think the lesion on the tongue and also the flat papules on the legs could fit in with a diagnosis of lichen planus.

Scleredema Adultorum (Buschke). Presented by DR. JULIUS GINSBERG.

Mrs. M. K., aged 24, had influenza the first week in October 1940; she was in bed three days and had a moderate fever. One week after getting up she noted stiffness and hardness of the neck and adjacent skin. The deep hardness, spreading peripherally from the neck, progressively involved the breasts and other areas of the body until a few weeks ago. The hands and feet were not involved. After the influenza subsided, she had rheumatism in her wrists, knees, left elbow and shoulder for about one month, although there was no local redness or swelling. Her mouth could not be opened more than about ¾ inch (2 cm.) until a few weeks ago because of the hardness of the tissues. During the first two months of her illness, her family physician prescribed sulfanilamide, desiccated thyroid, codeine and acetylsalicylate acid. Her influenza was in the nature of sore throat and "aching all over."

The results of routine laboratory tests on Dec. 13, 1940 were essentially normal.

Significant results of her physical examination include infected tonsils and blood pressure of 90 systolic and 68 diastolic.

For the past few weeks she has shown progressive improvement. The only treatment at present is heat and oil massage.

One biopsy specimen was fixed in Zenker's solution and the other in solution of formaldehyde U. S. P. diluted 1:10. The results were essentially the same. Special staining with mucicarmine and with cresyl (echt) violet, as recommended by Freund, did not demonstrate a mucin-like substance in the spaces apparent deep in the corium. Special elastic tissue and collagen stains revealed only some swelling of the collagen bundles.

DISCUSSION

DR. MORRIS WAISMAN (by invitation): A series of 15 cases of scleredema adultorum was reported from the Mayo Clinic last year (O'Leary, P. A.; Waisman, M., and Harrison, M. W.: Scleredema Adultorum, *Am. J. M. Sc.* **199**:458-466 [April] 1940). This rare disease follows an acute infection, usually one of the upper part of the respiratory tract, or an infectious exanthem. As a rule, a latent interval of several weeks intervenes between the acute episode and the onset of cutaneous changes. The induration appears first on the neck and quickly spreads to the face and over the trunk. In the case presented, as in the majority of cases, the hands and lower extremities are spared. One feature deserving mention is that muscular involvement may occur in scleredema, bringing up an additional point of confusion with the other dermatoscleroses—scleroderma and dermatomyositis. The

histologic changes have been reported as characteristic if one employs special stains (Freund, H.: Ueber Sklerödem (Buschke), *Arch. f. Dermat. u. Syph.* **161**:92-113, 1930). As in this case, however, my associates and I were never able to demonstrate in our material the mucin-like substance which has been described infiltrating among the collagen bundles.

Dr. Hamilton Montgomery, Rochester, Minn.: In scleredema histologically there is simply an edema between the collagen fibers, whereas in scleroderma there are sclerotic changes in the connective tissue and in the walls of the blood vessels. I am glad to hear that special stains were used in this case and that mucin could not be demonstrated. Patients with scleredema eventually get well in the course of several months. This patient is already improving. Occasionally, in the early or edematous phases of scleroderma and in the early stages of dermatomyositis, the clinical picture may closely simulate that of acute scleredema, and it may be necessary to observe the patient for some time before a final diagnosis is reached. Histologic studies are of distinct value in cases of this kind.

Dr. Udo J. Wile, Ann Arbor, Mich.: I had a patient with scleredema which was similar to the one presented. The condition began during pregnancy, the hands and feet were spared, and there was no tendency toward spontaneous involution of the lesions. One must not draw too fine a distinction with regard to prognosis in cases of this kind. In occasional cases the lesions do not undergo involution.

With regard to the confusion that exists in the differential diagnosis of these conditions, I do not think any one would confuse well developed scleroderma (with atrophy) with scleredema. Scleroderma beginning with edema and scleroderma in the edematous stage could easily be confused with scleredema.

Dr. Edward A. Oliver: I agree with Dr. Waisman that it is difficult to differentiate scleredema adultorum from the early stages of scleroderma. I presented a patient with this disease before this society about three years ago (Arch. Dermat. & Syph. **37**:694 [April] 1938). The patient was a large robust man whose condition was very acute and was preceded by a rather severe tonsillitis. I have since heard that he made an uneventful recovery in three to four months.

Dr. James R. Driver, Cleveland: There are a number of eruptions which are now recognized as vitamin deficiencies. My associates and I have a patient with dermatomyositis at present whom we are treating on the basis of its being a possible deficiency disease. We are giving this patient synthetic vitamin E (alpha tocopherol), and there has been a decided regression in the condition in about three weeks. I should consider the advisability of using this drug experimentally in cases of scleredema and scleroderma.

Dr. Carl W. Laymon, Minneapolis: The course of the disease in 2 patients I observed was much the same as that of this one. I should also like to emphasize what Drs. Waisman and Montgomery said concerning the difficulty of demonstrating the pseudomucinous substance in the tissues. Treatment does not seem to change appreciably the course of scleredema, although diathermy, massage, administration of salicylates and of thyroid and other measures have been used.

A Case for Diagnosis (Parapsoriasis?). Presented by Dr. David V. Omens and Dr. Harold D. Omens (by invitation).

F. S., a truck driver aged 53, presents a patchy erythematous eruption on the arms and legs of five years' duration. The patches are large, irregularly shaped, sharply defined and violaceous, with infiltration, scaling and some atrophy. On the arms the condition is reticulated. Itching is slight but noticeable at times.

The family history is negative. The patient states that he has had no illnesses except those of childhood.

The Wassermann and Kahn reactions were negative. The histologic picture was not incompatible with a diagnosis of parapsoriasis.

DISCUSSION

DR. HARRY R. FOERSTER, Milwaukee: I believe the condition in this case is parapsoriasis of the pityriasis lichenoides chronica type with the papulation not as well defined as one usually sees it and the reticulation more pronounced.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I believe this case is one of generalized atrophic lichen planus. The histologic structure is characteristic of lichen planus, having all the microscopic features of this disease and none of the characteristics of parakeratosis variegata. If the condition were parapsoriasis, microscopic examination would show parakeratosis variegata rather than parapsoriasis en plaques or pityriasis lichenoides chronica. The name parapsoriasis indicates parakeratosis histologically, which was not present in this case. In practically all cases of parapsoriasis a few sections show some evidence of parakerotosis, although lesions undergoing involution may show merely hyperkeratosis. Histologically, none of the three types of parapsoriasis reveals the typical histologic features of lichen planus which are present in this case.

DR. LESTER M. WIEDER, Milwaukee: I thought the presence of itching and the comparative freedom of involvement of the trunk were features against parapsoriasis in this case.

DR. OLIVER S. ORMSBY: If this condition is parapsoriasis it would have to be the parakeratosis variegata type. When working with Drs. Fox and McLeod I had the privilege of studying the case of parakeratosis variegata which formed the basis of their classification of parapsoriasis, which included parakeratosis variegata (originally described by Unna, Pollitzer and Santi), pityriasis lichenoides chronica (Juliusberg) and erythrodermie pityriasique en plaques disséminées (Brocq). This variety of eruption is usually generalized and retiform, the primary lesion being a reddish yellow or darker flat-topped scale-covered papule. The resemblance to lichen planus is sometimes striking. There is never any atrophy. In the case presented atrophy occurs and there is some itching; so the condition appears to be lichen planus with atrophy, not, however, the atrophic form of lichen planus which is characterized by white papules.

Lymphogranuloma Venereum. Presented by DR. HERBERT RATTNER and DR. MAURICE DORNE.

J. G., a Negro aged 40, presents multiple purulent draining sinuses of the penis and scrotum with associated bilateral inguinal adenopathy. The penis is edematous and indurated. The condition began about five months ago with the appearance of the sinuses on the penis. He entered the hospital because of urethral stricture. He had been receiving antisyphilitic treatment elsewhere and up to the time of admission to the hospital had received ten intravenous and ten intramuscular injections.

The rectal examination revealed no abnormalities.

The Kahn reaction was positive. Reactions to a Frei test and to a test for chancroid were positive. The results of urinalysis and of chemical examinations of the blood were normal. Roentgenographic examination of the chest, kidneys, ureters and bladder revealed no abnormalities. An electrocardiogram indicated probable myocardial damage.

The urethral strictures are not responding favorably to treatment by dilation. Consultants in the department of urology have raised the question as to the advisability of a cystotomy, and the patient is presented for discussion of that point.

DISCUSSION

DR. MAX S. WIEN: This man has three venereal diseases in addition to a sequela of lymphogranuloma venereum and numerous pigmentary residues in the forearms remaining from previous positive reactions to Frei tests. Before he

entered the hospital there was discharge from the glands in his groin, which subsided during his three weeks' stay after treatment with foreign protein and sulfanilamide. He has a type of elephantiasis of the penis reported by Stryker and Ploch (Elephantiasis of the Penis and Scrotum, ARCH. DERMAT. & SYPH. **32**:86-89 [July] 1935) and seen in 2 of the cases in the group studied by Dr. Perlstein and me at the Cook County Hospital, which we did not report. Our experience with this syndrome at Cook County Hospital was that the patients did poorly after any operative procedure and that it was better to control the venereal lymphogranuloma by appropriate treatment before any surgical treatment was instituted. In this case I think it woud be well to continue observation and therapy with foreign protein and sulfanilamide and to control the syphilis by proper treatment before starting treatment of the urethral strictures.

A Case for Diagnosis. Presented by DR. EDWARD A. OLIVER and DR. M. A. GOLD (by invitation), Hines, Ill.

W. H. F., a white man aged 62, states that in 1936 he noticed an eruption in the region of the left temple, which was yellow-brown and was associated with slight itching. It gradually became larger. In 1939, after an injury, it increased in size more rapidly, and at times he noticed pain in the left temple and in the scalp. This lesion was treated by "light therapy" without relief. He was admitted to the Veterans Administration Facility, Hines, Ill., for diagnosis and treatment.

On the left frontal region of the scalp is a flesh-colored, somewhat reddened lesion, ovoid in shape, measuring 10 by 8 cm., well circumscribed and minimally raised, with pitting edema. The center of the lesion is lighter in color than the periphery, and the edges appear to be slightly hemorrhagic.

The Wassermann and Kahn reactions were negative. The urine, the blood count and the results of chemical examination of the blood were normal. Repeated examinations of the sputum showed no fungi or tubercle bacilli. Cultures of material from the lesion showed no growth on media. Roentgenograms of the skull and chest were normal.

Histologic examination of the skin showed normal epidermis. The deeper layers of the corium consisted of hyalinized fibrous tissue. The hair follicles were elongated. Numerous lymphocytes and plasma cells and a few eosinophils infiltrated the tissue around the hair follicles.

DISCUSSION

DR. HARRY R. FOERSTER, Milwaukee: The indolent yellowish brown circumscribed infiltrate suggests that seen in chronic leukemia, though the results of examination of the blood do not support that diagnosis.

DR. JOHN F. MADDEN, St. Paul: I think that the lesion is probably the result of some degenerative process, such as colloid, amyloid or hyaline degeneration. It will be necessary to make several special stains before a diagnosis is possible.

DR. F. W. LYNCH, St. Paul: I agree with Dr. Madden.

DR. UDO J. WILE, Ann Arbor, Mich.: This case was most puzzling in its histologic picture. One would expect a most extensive cellular infiltrate, but there was little to be seen except a large number of bundles under the skin which appeared to be fixed connective tissue, but they looked rather odd. I am reminded of a patient I showed before this society many years ago with plaquelike lesions of this sort on the breast. The lesions looked like keloid and under the microscope showed similar bundles resembling connective tissue. On making a special stain, however, I found that they were made up of nerve fibers. Would it not be a good idea before a diagnosis is definitely made to have a histologic section stained for nerve tissue, to make sure these bundles are not composed of nerve elements?

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I thought that histologically this case was one of colloid degeneration of the skin. After discussing the case with Dr. Wile, I again studied the slides for evidence of nerve fibers, and I agree with Dr. Wile that special stains should be used. I suggest Van Gieson's stain to distinguish connective tissue from smooth muscle and the Bodian stain, which in my experience has been specific for nerve fibers and does not stain the reticulum or lattice fibers. From the clinical standpoint, one must also consider localized myxedema, but histologically there is no bluish stain of mucin-like substances with the hematoxylin and eosin stain. Amyloid stains similarly to colloid but frequently shows involvement of the walls of the blood vessels, which is not present in this case. The same is true of lipoid proteinase with extracellular deposits of phosphatides and other lipoids seen in the latter condition. I have observed cases of colloid degeneration of the skin in which the nuclei of the degenerating collagen fibers still persisted. I could not see evidence of any definite nerve fibers, and I still support a diagnosis of colloid degeneration of the skin subject to what one finds with special stains.

DR. UDO J. WILE, Ann Arbor, Mich.: Does the patient have pain?

DR. EDWARD A. OLIVER: The lesion is not painful.

According to the patient's history, a lesion about the size of a quarter began to develop in 1936. He bumped the lesion on a fence post in 1939 and then noticed its gradual progression.

Dermatitis Herpetiformis. Presented by DR. EDWARD A. OLIVER and DR. T. M. COHEN (by invitation).

W. J., a Negro aged 38, presented from a clinic at the Northwestern University Medical School, has a vesiculobullous eruption of fourteen months' duration. It appeared first on the chest and then on the back of the neck, the trunk and the extremities. Throughout the course crops of lesions have recurred accompanied by intense itching. In June 1940 the patient was hospitalized and given 40 grains (2.6 Gm.) of sulfapypridine (2-[paraaminobenzenesulfonamido]-pyridine) daily. In ten days the eruption had cleared completely. A section of the skin showed a picture indicative at that time of dermatitis herpetiformis. His skin remained clear until December 1. He is now presented to show the extensive depigmentation of areas that were previously the sites of active lesions.

Laboratory examination of the urine and blood showed no abnormalities.

DISCUSSION

DR. H. J. PARKHURST, Toledo, Ohio: I was interested in the great improvement apparently due to the administration of sulfapyridine, similar to the striking improvement in a case presented last year by Dr. Senear (A Case for Diagnosis [Dermatitis Herpetiformis in a Child?], ARCH. DERMAT. & SYPH. **42**:198 [July] 1940; in discussion on Omens, D. V.; Reifler, R., and Falk, A.: Dermatitis Herpetiformis, ibid. **43**:1065 [June] 1941).

Telangiectasia Hemorrhagica Hereditaria (Osler's Disease) and Vitiligo. Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

F. Y., a Jugoslavian aged 58, complains of red patches on his skin which have been present for more than twenty years. He states that his mother had the same condition. There is some itching associated with the lesions. He has, in addition, frequent hemorrhages from the nose and has experienced some difficulty in stopping these and other hemorrhages, accidental in nature.

Examination shows many telangiectatic areas of various sizes and shapes on the lips, nose, cheeks, ears, oral mucosa, nasopharynx, lower parts of the arms and

dorsa of the hands. In addition, there are several areas of depigmentation of varying size, the largest one being located on the anterior aspect of the neck.

Examination of the blood showed 6.3 Gm. of hemoglobin per hundred cubic centimeters, 3,630,000 erythrocytes and 6,000 leukocytes. The bleeding time was three minutes and thirty seconds. The clotting time was three minutes and five seconds. There were 490,000 platelets. Examination of the stools showed strongly positive reactions for blood. The urine was normal.

Treatment has been started with thorium-x locally and ferrous gluconate by mouth.

DISCUSSION

DR. A. W. STILLIANS: This condition is a typical example of telangiectasia haemorrhagica hereditaria.

DR. WESLEY WILSON (by invitation): This case was presented as a typical instance of Osler's disease. The simultaneous presence of the same syndrome in the patient's mother is an additional feature of interest.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

H. V. ALLINGTON, M.D., *President*

ERVIN EPSTEIN, M.D., *Secretary-Treasurer*

Feb. 7, 1941

A Case for Diagnosis (Dermatitis Medicamentosa?). Presented by DR. FREDERICK G. NOVY JR., Oakland, Calif.

M. M., a 52 year old Mexican laborer, came to the University of California dermatologic clinic on Jan. 21, 1941, complaining of an eruption on his face and on his upper extremities of one year's duration. At the time of onset he consulted a physician, who made a diagnosis of latent syphilis. At that time he also had an eruption on his face of unknown cause, possibly a contact dermatitis.

During the past year the patient has had forty injections of a bismuth preparation and nineteen injections of mapharsen. The eruption has undergone exacerbations every two weeks, characterized by intense itching of the eyelids, face and upper extremities. The patient stated the belief that the eruption is accentuated after each injection of mapharsen and that when the condition is aggravated, the eruption assumes a vesiculopapular character. Oral lesions are common, particularly on the lower lip.

A patch test with a solution of mapharsen was applied on January 21 to a region on the left forearm adjacent to the eruption. Twenty-four hours later the patient removed the patch and found the tested area to be definitely vesicular. When it was examined at the clinic a week later, the area showed confluent pigmented papules.

The results of a physical examination were normal. The urine and blood count were normal, platelets being 450,000 per cubic millimeter. Liver function, as measured by the rose bengal test, was normal.

The patient has taken no other medication regularly. A test dose of a preparation containing phenolphthalein was taken yesterday.

The lesions now consist of excoriations, lichenification and pigmentation, with deeply pigmented macules and an occasional depigmented macule. There are lighter pink areas in the vermilion portion of the lower lip.

DISCUSSION

DR. F. G. NOVY JR., Oakland, Calif.: The patient states that the eruption around his neck is worse today. The lesions on the forearms, however, have not shown any increased activity. I have never seen this type of lesion develop from phenolphthalein. He has had no mapharsen for four weeks. I still cannot make a definite diagnosis.

Papulonecrotic Tuberculid. Presented by DR. H. E. MILLER.

L. C., a white woman aged 37, was presented at the meeting of the society on April 19, 1940 (ARCH. DERMAT. & SYPH. **43**:714 [April] 1941).

In January 1941 the patient returned to the clinic with an indolent pustule on the knee.

Fig. 1.—*A*, papulonecrotic tuberculid on the leg. *B*, healed reaction to a tuberculin test.

DISCUSSION

DR. H. J. TEMPLETON, Oakland, Calif.: I was particularly interested in the scar on the arm, which, if I understood clearly, is the result of a tuberculin reaction and of course indicates a high degree of sensitivity to the tubercle bacillus. It reminds me of histologic slides that I saw in Kerl's clinic showing the gradual development of the typical pathologic picture of papulonecrotic tuberculid at the site of injection of old tuberculin in tuberculin-sensitive patients.

DR. F. G. NOVY JR., Oakland, Calif.: Are all patients with papulonecrotic tuberculids hypersensitive to tuberculin, and can they be desensitized? I have a patient who still gives strong local reactions after six months of attempted desensitization.

DR. H. E. MILLER: This patient, as you will recall, had a diagnostic tuberculin test done fifteen months ago. She has a scar the size of a 50 cent piece on her forearm which resulted from it. Her skin had been clear prior to that time, but a few weeks after the test was performed papulonecrotic lesions developed on her extremities. Dr. Goldsmith (Goldsmith, W. N.: Recent Advances in Dermatology, P. Blakiston's Son & Co., 1936, p. 270) reported observing showers of tubercle bacilli in the blood stream after diagnostic injections of tuberculin. Such a sequence of events apparently took place in this patient and accounts for her cutaneous lesions. Dr. Goldsmith (ibid., p. 282) stated that

sensitiveness to tuberculin in patients with tuberculids is less than in those with true tuberculosis of the skin.

Pemphigus Foliaceus. Presented by Dr. Norman N. Epstein.

F. R., a white single man aged 55, a waiter, entered the San Francisco Hospital on Nov. 23, 1940.

The patient was well until three weeks before entry, at which time blisters appeared on both wrists while he was handling cement, working on a WPA street project. Subsequently lesions appeared spontaneously on the forearms, hands, neck and scalp, in the axillas and finally on the flanks. The lesions start as painful blisters which dry and desquamate without scarring.

He has had no previous similar illness or eruption. The patient has mild chills at night but otherwise feels well.

Treatment has consisted of the administration of sulfanilamide blood transfusions, potassium permanganate baths and the administration of vitamins (thiamine hydrochloride, nicotinic acid and vitamin D.

Cultures of material taken from the bullae on December 20 showed hemolytic Staphylococcus aureus and beta hemolytic streptococci. On Jan. 30, 1941 a similar culture showed hemolytic Staph. aureus. A differential count performed on the fluid from the bullae showed 48 per cent polymorphonuclear leukocytes, 4 per cent basophils, 40 per cent eosinophils and 8 per cent lymphocytes. Kolmer and Kahn tests gave negative results. A blood count showed 17,000 white blood cells, 78 per cent hemoglobin and 75 per cent polymorphonuclear leukocytes. The urine was normal.

With the administration of sulfanilamide the hemoglobin dropped to 42 per cent; so this therapy was discontinued, although the lesions had improved. After this new lesions formed on the legs, and the administration of sulfanilamide was resumed. The patient has had two transfusions since.

DISCUSSION

Dr. Merlin Maynard, San Jose, Calif.: A woman 82 years old had pemphigus four months ago. I considered her condition fatal twice. Therapy consisted of large doses of vitamin D. The first vitamin B complex I gave her had no effect on the lesions on the mucous membranes; so later I gave her riboflavin. I feel that probably all the vitamin B complex preparations on the market are not to be relied on for full riboflavin effect. Her tongue is normal now, and, except for a little difficulty in walking due to an arthritic condition, she is well.

Dr. N. N. Epstein: One of the main reasons for presenting this case was to bring up a discussion of therapy.

Sulfanilamide has been reported as having a definite effect on pemphigus. On entry to the San Francisco Hospital this patient was given 90 grains (5.8 Gm.) of sulfanilamide daily for a week. His temperature rose to 105 F., and he became sick; so this therapy was discontinued. During the time he took sulfanilamide every blister disappeared. However, when administration of the drug was stopped the lesions reappeared. He was given sulfanilamide again. No new bullae appeared for a number of days. However, anemia developed, so administration of the drug was stopped, and the lesions reappeared. He was given sulfanilamide again, with no decided beneficial effect.

Note.—Large doses of vitamin D are being given, as well as sulfathiazole. The patient's condition on March 1, 1941 is good, and bullae have not appeared for a few days.

A Case for Diagnosis (Ulcer of the Hand). Presented by Dr. H. V. Allington, Oakland, Calif.

T. P., a white woman aged 20, was first seen on Nov. 13, 1940, because of an area of necrosis involving about two thirds of the dorsal surface of the right

hand. This is said to have begun as the result of a bite of a small brown spider on November 4. It was treated with tincture of iodine and by soaking in magnesium sulfate solution and later by the application of wet dressings of potassium permanganate solution. A tough black adherent eschar formed rapidly. On November 12 new areas of necrosis developed on the proximal margin and extended into the middle two interdigital spaces. The margins of the ulcer were abrupt and showed a relatively narrow inflammatory zone. The outline was bizarre, and about the base of the fingers there was a linear or streaked appearance. Occlusive wet dressings of physiologic solution of sodium chloride were advised, and the patient was treated by Dr. R. J. Walker, of Oakland, Calif. No further spread occurred, and by the middle of January 1941 the area had healed. It remained healed only a few days, and then the central portion of the scar became necrotic, this time without a history of trauma.

The patient's general health has been good. The result of a Kline test was negative. Examination of the blood showed 85 per cent hemoglobin, 5,000,000 erythrocytes and 8,650 leukocytes, with a differential count of 53 per cent polymorphonuclear leukocytes (including 4 per cent stab cells), 46 per cent lymphocytes and 1 per cent eosinophils. Cultures of material removed from the ulcer showed Staphylococcus aureus and Streptococcus viridans.

DISCUSSION

DR. H. E. MILLER: I should consider the lesions to be self inflicted until proved otherwise. The physician who has the patient under his constant care can decide this point much better than one who sees the patient for a minute or two at a meeting of this type.

DR. HARRY E. ALDERSON: I had the same impression, owing to the fact that she has hypertrophic scars from former injuries. I asked about her occupation, having in mind the compensation factor, and she said she was a housewife.

DR. F. H. STIBBENS, Oakland, Calif.: She is a housewife but has been for only five months.

DR. A. E. INGELS: It would interest me to know what kind of protective dressing was used.

DR. H. V. ALLINGTON, Oakland, Calif.: Plaster dressings were not used. Gauze and adhesive tape were used in such a manner as to make their removal impossible without detection. The patient was married recently and lives with her husband and mother-in-law.

Glossitis Rhomboidea Mediana. Presented by DR. EDWARD A. LEVIN.

A white woman aged 48, a housewife, first noted changes on the middle third of the dorsal surface of her tongue two years ago. At present there is a rhomboid, indurated, smooth patch, about 1 cm. in diameter, in this location. The condition is asymptomatic. The patient has had no treatment. The Wassermann reaction was negative. A roentgenogram of the chest and a complete blood count were found to be normal.

DISCUSSION

DR. N. N. EPSTEIN: I saw this patient before Dr. Levin proposed this diagnosis. She came into the clinic because of this infiltrated plaque. I felt that the possibility of its being one of the chronic granulomas had to be ruled out. Complete examination, including a biopsy, failed to reveal any evidence of this group of diseases.

DR. EDWARD A. LEVIN: McCarthy (McCarthy, F. P.: A Clinical and Pathologic Study of Oral Disease, *J. A. M. A.* **116**:16 [Jan. 4] 1941), in a recent study of lesions of the tongue, reported an incidence of about 1 per cent for this entity. The condition seems to be rare.

A Case for Diagnosis (Ariboflavinosis?). Presented by Dr. Ervin Epstein, Oakland, Calif.

E. L., a 54 year old white man, was first seen on Dec. 21, 1940, because of an eruption of his face, neck and scalp of two years' duration. The lesions were asymptomatic. He had been treated by a dermatologist during the preceding four or five months for dermatitis venenata. Positive reactions to cutaneous tests had been obtained with certain clays and plasters that he contacted in his work as a molder. He had done this type of work for ten years prior to the onset of the cutaneous complications. Local and roentgen ray therapy had been ineffectual in eradicating the eruption. He stated that he was not addicted to the use of alcohol. The patient's diet was well balanced, including such riboflavin-containing foods as liver, wheat, eggs, carrots, cheese, milk and kale.

The patient presented an erythematous, plaquelike eruption in the aforementioned locations. He had two large paranasal lesions with superimposed crusting. Fissuring of the corners of the mouth was accompanied by erythema and crusting extending onto the cutaneous surface. Smaller similar plaques were present on his neck and scalp. There was no dandruff on his scalp. His tongue was red and smooth.

Therapy was instituted with the administration of vitamin B complex, 15 cc., and nicotinic acid amide, 300 mg., orally each day. One week later he showed 75 per cent improvement. He then discontinued taking the vitamin B complex, and there was a prompt recurrence of the cutaneous lesions. The improvement of the tongue continued with the ingestion of the nicotinic acid amide. The vitamin B therapy was reinstituted, but it was found that daily doses of 5 cc. and of 10 cc. were insufficient to control the eruption satisfactorily. Two days ago, these measures were discontinued, and the patient was given 9 mg. of riboflavin daily. There has been a great improvement during this time.

The patient has also used 5 per cent ammoniated mercury ointment locally and has received a total of 170r of superficial roentgen radiation with no appreciable effect on the eruption. During the past few days an acute dermatitis of the scrotum has developed, which the patient attributes to the clay and plaster dust which works its way under his pants.

DISCUSSION

Dr. H. E. Miller: A diagnosis of ariboflavinosis does not seem justified from the data presented. It was stated that the eruption was asymptomatic. The patient said that it itched. I think that one might obtain some additional worth while information by making an analysis of gastric contents.

Dr. H. J. Templeton, Oakland, Calif.: I wonder also whether the improvement might have been due to the roentgen ray therapy that was given.

Dr. Ervin Epstein, Oakland, Calif.: I agree with Dr. Miller that the diagnosis is not definite. The patient had consistently stated that there was no pruritus except on the scrotum, and the lesion here is a new one. The patient should have an analysis made of gastric contents. When I first saw him, I considered the possibility of a malignant condition of the stomach interfering with absorption of the vitamin. However, the cutaneous lesions have been present for two years, and one would expect some loss of weight in this length of time. Regarding the roentgen ray therapy, the patient had a considerable amount of this before I saw him. The patient's diet is apparently adequate in riboflavin. Some patients may require a larger amount of a given vitamin than others. It is interesting that doses of vitamin B complex in excess of the average maintenance dose did not prevent a recurrence of the lesion. Despite the clinical picture and the apparent response to the administration of riboflavin, the possibility of an industrial dermatitis must be given further consideration.

Note.—Riboflavin in doses of 9 mg. daily failed to cure this patient completely.

Parapsoriasis en Plaques. Presented by DR. MERLIN MAYNARD, San Jose, Calif.

V. G., a 37 year old white man, had an eruption on the cheeks and scalp for one and one-half years. Recently the process has spread to his body. He has been a refrigerator salesman for fifteen years. His general health has been good. He drinks and smokes moderately.

The patient states that the eruption is slightly pruritic and is more severe than usual at present. It is more evident after exposure to sunlight. He has complained of indigestion recently. Various local remedies have been prescribed by his local family physician. Examination of the blood showed a mild secondary anemia but no other abnormalities. The results of a fractional analysis of gastric contents were also normal.

Examination of the patient shows a number of roughly circular areas on the scalp from which the hair may be pulled with ease. The hair roots are moist and not of the exclamation point type. The cheeks feel infiltrated. A plaque in the center of the right cheek contains several nodules. Scattered over the trunk are numerous oval plaquelike areas, 6 to 8 cm. in the long axis. They are slightly reddened and covered with a light scale. Histologic examination showed only moderate acanthosis. The histologic appearance was consistent with a diagnosis of parapsoriasis.

DISCUSSION

DR. A. E. INGELS: I feel that one can call almost any eruption parapsoriasis. The histologic picture in this case is not diagnostic of parapsoriasis and excludes mycosis fungoides. I should investigate the case further. Dermatitis venenata might play some role.

DR. H. J. TEMPLETON, Oakland, Calif: This condition is a chronic maculopapular, resistant, scaly erythroderma, which is the morphologic description of parapsoriasis.

DR. N. N. EPSTEIN: I think that before one applies the term parapsoriasis to this patient's eruption time should elapse to prove that it is a resistant erythroderma. I was interested in the alopecia. I was not able to connect that with his eruption. It is probably alopecia areata.

DR. ERVIN EPSTEIN, Oakland, Calif.: I should like to inquire whether photosensitivity is not unusual in either parapsoriasis or mycosis fungoides. Owing to the fact that the patient's eruption is atypical and that he handles a fluorescein derivative, I suggest the possibility of the eruption being a dermatitis with photosensitivity due to fluorescein.

DR. W. M. MEININGER: The lesions on the trunk correspond to those of Brocq's en plaque type of parapsoriasis. The ham-colored, arciform, indurated lesions on the right cheek do not fit into this picture; they may represent an early stage of mycosis fungoides. They are suggestive of tertiary syphilis, and a serologic examination should be made.

DR. MERLIN MAYNARD, San Jose, Calif.: I believe that the condition in this case should be classified as a scaly erythroderma. From the appearance of the lesion on the right cheek, I believe it is in a transitional stage toward mycosis fungoides. In support of this conclusion is the beginning infiltration of the cheek and the fact that during the past few months itching has commenced. The condition can be called parapsoriasis en plaques because it resembles descriptions of that entity as given in textbooks. However, time will reveal the true diagnosis, and I suspect that it may be mycosis fungoides. The alopecia looks like the areata type. The sheath comes out, however, when the hair is pulled, and that is not characteristic of alopecia areata. The patient is exposed to hydrochlorodifluoromethane, but only infrequently.

DR. F. H. STIBBENS, Oakland, Calif.: The patient is also exposed to refrigeration.

Scleroderma (Morphea). Presented by DR. H. V. ALLINGTON, Oakland, Calif.

E. H. R., a white woman aged 53, consulted me on January 27, 1941 because of lesions in the armpits, beneath the breasts, on the right side of the chest and in the crural folds. These began about six months ago. They have been accompanied by a mild intermittent pruritus. They are dull, whitish, superficially infiltrated patches, with smooth, slightly elevated margins, and vary in size up to 4 by 10 cm. The central portion of the larger lesions in the armpits and crural folds are slightly depressed and have a grayish, wrinkled, scaling surface. The lesions on the trunk are guttate in type. None show the characteristics of lichen planus. The patient's general health has been good. She has been under unusual physical and mental stress during the past year.

The result of a Kline test was negative. The histologic picture is, I believe, compatible with a diagnosis of scleroderma.

Two ¼ skin unit doses of roentgen rays have been given, and treatment with an insulin-free pancreatic extract has been started.

Scleroderma (Morphea with Early Vesiculation). Presented by DR. H. V. ALLINGTON, Oakland, Calif.

E. G., a 53 year old woman, was first seen on Jan. 23, 1941 because of lesions which began one and one-half years ago and have been gradually enlarging. They now consist of four ivory-colored patches symmetrically placed on the shoulders at the margins of the trapezii and in the supraclavicular fossae. Those at the margins of the trapezii are roughly circular, about 7 cm. in diameter; the others are oval and about 3.5 by 7 cm. in size. There are smaller guttate lesions scattered near the larger ones. The lesions are superficially infiltrated. Covering practically all of the lesions on the right trapezius is a shallow, thick-walled, multilocular bulla, the content of which is apparently thick, drying serum and old blood. This lesion rises slightly above the level of the surrounding skin and is a variegated reddish purple. In the other larger lesions there are small areas of this discoloration, suggesting slight superficial hemorrhage and abortive vesicle formation. In the center of these lesions the epidermis is thickened and wrinkled, looking as though it might shortly peel off. The change in color has developed during the past few weeks. Prior to this the lesions had been white and had attracted less attention.

The patient's general health has been excellent. A complete physical examination by Dr. Francis Kearney, of Hayward, Calif., showed no significant abnormality.

The result of a Kline test was negative. Examination of the blood showed 4,580,000 red blood cells, 8,850 white blood cells, 85 per cent hemoglobin and a color index of 0.9, with 66 per cent polymorphonuclear leukocytes (including 11 per cent stab cells) and 34 per cent lymphocytes.

Treatment has consisted of the administration of 50,000 U. S. P. units of vitamin A daily and injections of an insulin-free pancreatic extract twice weekly.

DISCUSSION OF TWO CASES OF SCLERODERMA (MORPHEA)

DR. A. E. INGELS: I feel that the condition in these cases does not fall into the scleroderma group but is rather lichen sclerosus et atrophicus. The patients both presented small angular nodular lesions on the head with a cigaret-paper-like, atrophic consistency. I feel that the histologic structure is not that of scleroderma but that of lichen sclerosus et atrophicus. This brings one back to the dispute as to whether these conditions are the same or are varieties of the same disease.

DR. H. J. TEMPLETON, Oakland, Calif.: I am inclined to agree with Dr. Ingels. I felt that the first of the 2 patients had a disease of the lichen sclerosus et atrophicus group.

DR. F. G. NOVY JR., Oakland, Calif.: Does this patient take any internal medication?

DR. A. E. INGELS: I should be interested in seeing histologic sections stained for collagen and elastin.

DR. H. V. ALLINGTON, Oakland, Calif.; The patient takes no drugs except an occasional dose of alka seltzer.

Localized Scleroderma. Presented by DR. CHARLES ALBERT SHUMATE.

M. J. R., an 8 year old girl, is presented from the clinic of St. Mary's Hospital.

Extending from the hair line on her forehead to her eyebrows is a depressed atrophic area which was first noticed several years ago. For the past eight months there have been on the right side of her face firm, smooth, round white patches, averaging 4 cm. in diameter.

There are no subjective symptoms. Her general health is good. A physical examination showed only normal results.

Her basal metabolic rate was + 8 per cent on Feb. 5, 1941. A roentgenogram of the head on the same date was reported by Dr. John O'Neil of St. Mary's Hospital as showing no abnormalities. Histologic sections were consistent with a diagnosis of scleroderma.

DISCUSSION

DR. F. G. NOVY JR., Oakland, Calif.: Dr. Allington, do you think this condition is the same entity as that in the cases you just presented?

DR. H. V. ALLINGTON, Oakland, Calif.: The patient reminds me very much of one I presented (ARCH. DERMAT. & SYPH. **41**:437 [Feb.] 1940) with hemiatrophia faciei. She was a woman 35 years of age whose lesions began when she was in the early teens. Her condition was one of atrophy only, and I think that this girl will probably ultimately show atrophy only. This convinces me that facial hemiatrophy, in some cases at least, is simply an end result of scleroderma.

DR. H. E. MILLER: Some dermatologists have had medicolegal difficulties with lesions of this type. The parents of the patient should be told the outcome of the condition without treatment, and no local therapy should be undertaken.

DR. ALBERT SHUMATE: One of the reasons I presented this typical case was to get ideas about treatment. If there are any suggestions, I should appreciate receiving them.

DR. H. J. TEMPLETON, Oakland, Calif.: An insulin-free extract of pancreas was being given when the condition of one of my patients cleared up.

DR. MERLYN MAYNARD, San Jose, Calif.: I have treated 4 patients with localized scleroderma with vitamin D. I have just dismissed the last one as being healed. I suggest that this child be given vitamin D and a low calcium diet for as long as necessary—even six months to a year—to prove the value or lack of value of this therapy for her. In 1 of my cases it took three or four months and in another as long as eighteen months for the condition to subside. I think one makes a mistake if one does not consider the physiologic basis of scleroderma, which is an increased calcium deposit. Therefore, in scleroderma the administration of vitamin D is the rational and successful therapy. Ammonium chloride also mobilizes the calcium.

Hereditary Alopecia. Presented by Dr. H. J. Templeton, Oakland, Calif.

W. G., aged 21, consulted me on Dec. 26, 1940, complaining of alopecia of the scalp, which had begun when he was 8 months old. The hair was lost gradually, until now only some tufts remain above his ears. His eyebrows, beard, chest, back and pubic areas have a normal amount of hair. There is no hair in the axillas. His legs have a scanty amount of hair.

Figure 2 presents the hereditary picture, showing a tendency transmitted through the female to the male descendants but apparently not transmitted through the males.

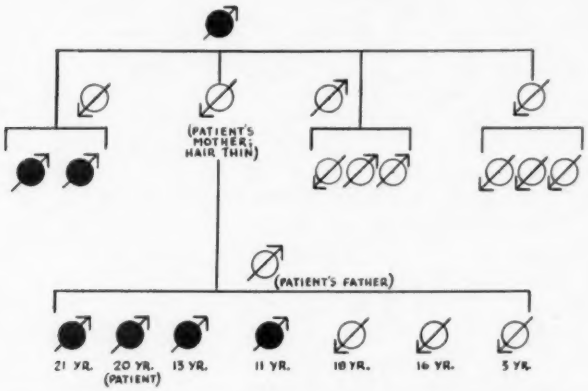


Fig. 2.—Diagram of the hereditary background of a patient with alopecia. The open symbols indicate normal persons; the filled-in symbols indicate bald persons.

DISCUSSION

Dr. H. J. Templeton, Oakland, Calif.: I thought that this case was unusual. It seems to show a hereditary defect which has passed through the female sex to the male offspring.

Progressive Scleroderma. Presented by Dr. Frances A. Torrey.

Mrs. R. W., a Russian housewife aged 50, entered the University of California Hospital on Feb. 2, 1941, with the following complaints: increasing deafness for six years; intermittent pain in the finger tips for five years; increasing pigmentation of the left forearm, chest and face, followed by tightening of the skin for eight months, and difficulty in walking, with pain in the thighs for three months.

Physical examination shows a thin, afebrile woman with redness, thickening and induration of the skin of the right and left forearm and of the chest. There is a zone of brownish pigmentation outlining the induration on the right forearm. The chest shows multiple small oval white atrophic areas. The skin of the hands is tight and smooth with flexure contraction of the fingers. There are healing ulcers at the tips of both index fingers. The face appears immobile, and the skin of the nose and cheeks is reddish and indurated. Changes in the feet and toes are minimal. Analysis of the gastric contents showed no free acid in specimens of the alcohol meal. Occult blood was present in the fasting gastric content, but no lactic acid was demonstrated. The free hydrochloric acid was 30 half an hour after the administration of histamine phosphate. The ascorbic acid level of the plasma was 0.19 mg. per hundred cubic centimeters.

Examination of the blood showed 90 per cent hemoglobin, 4,900,000 red blood cells and 7,950 white blood cells, with 66 per cent polymorphonuclear leukocytes, 10 per cent eosinophils, 20 per cent lymphocytes and 4 per cent monocytes.

DISCUSSION

DR. ERVIN EPSTEIN, Oakland, Calif.: It is interesting to consider this case in the light of the statement made by Dr. Maynard in discussing a previous case. While some dermatologists feel that calcium metabolism is the primary defect in scleroderma, others consider the cause of this disease to be vascular. In 3 cases of generalized scleroderma, fever therapy led to varying degrees of improvement, ranging from slight to definite. Perhaps these results were due to increased circulation. Thyroid may give the same effect rather than any specific endocrine action. The effect of insulin-free pancreatic extract is also believed to be due to increase of local circulation. In 1 patient therapy with a passive vascular exercise apparatus (pavaex) applied to the arms and legs led to definite improvement. For this reason I suggest treating this patient with a passive vascular exerciser or with the tissue extract mentioned by Dr. Templeton.

In studying 2 cases of calcification of otherwise normal skin, it appeared that the circulation was decreased in the area of deposition. In one case capillary microscopic examination revealed large tortuous capillaries with a sluggish circulation. In the other photographs taken with infra-red rays showed large blood spaces. While it is impossible to judge the rate of flow in such photographic investigations, the pictures suggested that pools of blood were formed.

DR. MERLIN MAYNARD, San Jose, Calif.: If slowing of the circulation were a factor, one would expect to find calcification in other areas, such as varicose veins. That might be an argument against the slowing of the circulation causing deposits of calcium.

DR. ERVIN EPSTEIN: I did not mean to imply that sluggish circulation was the only factor in calcification of the skin, but a study of these cases suggested that it was a factor which might act in the same way to cause an increased deposit of calcium in the sclerodermatous tissue.

DR. MERLIN MAYNARD, San Jose, Calif.: The most extensive condition for which I gave vitamin D was that of a woman 38 years old who had large plaques, as large as my hands, on the breasts and thighs. My experience has been with relatively localized conditions, but I believe that a response could be expected in more generalized conditions as well.

DR. FRANCES A. TORREY: It would be interesting to hear some discussion on scleroderma versus acrosclerosis versus dermatomyositis.

The patient's lesions began on her fingers with symptoms like those of Raynaud's disease. Then the scleroderma spread over her arms, as Sellei has described in acrosclerosis (Sellei, J.: The Diagnosis and Treatment of Scleroderma and Acrosclerosis, *Brit. J. Dermat.* **46**:523, 1934). The calcium content of her blood is within normal limits. In this condition there is devitalized tissue. It has been pointed out by Bolam that this degenerative change includes a change in the fat lobules, and he suggested that this primary local change is the basis for the calcium deposition (Bolam, M.: Calcinosis, *Brit. J. Dermat.* **47**:340, 1935).

DR. ERVIN EPSTEIN: Regarding the relation of dermatomyositis to scleroderma, muscle involvement must be very common in scleroderma. In 6 consecutive patients with scleroderma creatinuria was demonstrated in amounts in excess of the normal (Epstein, E., and Ayres, S., Jr.: Cretinuria in Scleroderma, *J. Lab. & Clin. Med.* **22**:697 [April] 1937). I believe that this indicates muscle involvement. While it does not demonstrate an etiologic relation between the two diseases, it suggests that muscular changes commonly occur in scleroderma as well as in dermatomyositis.

DR. FRANCIS A. TORREY: Dowling has investigated that phase of the subject and has found a close similarity in the degenerative changes in the muscle in dermatomyositis and in scleroderma. He also reported the same changes in cer-

tain patients with thyrotoxicosis and myasthenia gravis (Dowling, G. B.: Generalized Sclerodermia, *Brit. J. Dermat.* **52**:242, 1940; Dowling, G. B., and Griffiths, W. J.: Dermatomyositis and Progressive Scleroderma, *Lancet* **1**:1424-1428, 1939).

Dermatitis Herpetiformis. Presented by DR. NORMAN N. EPSTEIN.

G. K., a 47 year old railroad employee, entered the University of California Hospital complaining of a severely pruritic eruption of seven weeks' duration. The patient has had diabetes for several years, which is well controlled. His general health is excellent.

The eruption is symmetrically distributed over the shoulders, the flexor and extensor aspects of the elbows, anterior aspects of the legs, the buttocks and the genitalia. It is characterized by exacerbations and remissions. The lesions reappear suddenly. There are discrete and confluent papules, vesicles and small bullae, with large, coalescent, macerated areas resulting from rupture of the bullae.

Since the patient entered the hospital on Jan. 28, 1941, he has received 6 Gm. of sulfanilamide daily, as well as topical applications, including a starch lotion, 1 per cent ammoniated mercury in cold cream and starch baths. These have given him some comfort, but new lesions have continued to appear.

The urine is normal. The blood is normal except for 6 per cent eosinophils.

DISCUSSION

DR. N. N. EPSTEIN: This patient has been treated with sulfanilamide in much larger doses than has been reported in the literature. I do not think that one can say that the patient derived much benefit from it. It is interesting that, although dermatitis herpetiformis and pemphigus are clinically related diseases and at times indistinguishable, after a comparison of the condition in this case and in the case of pemphigus presented this evening there could be no question but that they are distinct entities. In typical cases the two diseases are different, although in borderline cases they may be impossible to distinguish.

Acrodermatitis Chronica Atrophicans. Presented by DR. NORMAN N. EPSTEIN.

A white man aged 49, born in Russia, presents a slowly progressive reddening of the anterior portion of each leg extending from the dorsum of the foot to above the knee. The skin in these areas is indurated and boardlike in consistency. Over each knee and elbow the skin is atrophic and reddened, producing a cigaret-paper-like consistency.

The patient's main complaint is severe intermittent pains in the legs, which are unrelated to walking and are most severe at night. These pains have increased in severity during the past few months.

The results of routine laboratory examinations were normal.

DISCUSSION

DR. H. E. MILLER: I agree with the diagnosis.

DR. MERLIN MAYNARD, San Jose, Calif.: I saw this patient in my office a year or so ago. I gave him vitamin D, but apparently there was no improvement.

DR. HARRY E. ALDERSON: I have seen considerable improvement in a similar case studied at Stanford Clinic, in which a nerve block operation was done.

DR. N. N. EPSTEIN: This man complains of a great deal of pain. I wonder whether this is common in cases of this kind. In a case presented a few years ago, the patient did not have pain.

DR. F. G. NOVY JR., Oakland, Calif.: I do not believe that the presence of pain is uncommon.

Keloids. Presented by Dr. Harry E. Alderson.

W. C., a 41 year old Negro porter, was examined at the Stanford dermatologic clinic of the University Hospital, and a diagnosis of scabies was made. He was found to have large keloids on his chest and abdomen and in old vaccination scars. The patient stated that he has had keloids ever since he was a boy. Recently he has noticed intense pruritus of the keloids on his chest. There has been a gradual extension of the keloids in the last year, especially of the lesions which he scratches most frequently.

It is interesting to note that the traumatic scars on his left hip, which he has had for thirty years, do not show keloidal tendencies. The Wassermann reaction was negative.

DISCUSSION

Dr. A. E. Ingels: The most interesting aspect of this case is the circinate polycystic configuration of the keloids, which indicates that the patient probably has come through the tertiary stage of syphilis with keloidal scar formation fixing the outline of the healed syphilitic lesions.

Dr. Harry E. Alderson: It is interesting that the patient gives no history of traumatism in any place where keloids appear other than the vaccination sites. On the hip, where he did have trauma, there is a little scarring but no keloid has appeared. Naturally, I do not plan to treat this man, but I should like to receive suggestions as to treatment in cases in which the lesions are less numerous. It is well known that keloids often assume bizarre and circinate forms.

Telangiectasia. Presented by Dr. C. J. Lunsford, Oakland, Calif.

Miss E., aged 23, a student at the University of California, presents on the right arm and forearm a mosaic of closely packed fine blood vessels, some of which do not fade on pressure. These are most evident on the flexor surface and have been present since she was in primary school. The patient states that the lesions near the right wrist have developed within the last year.

On the right side of the right breast, coursing over the shoulder, are similar lesions, which have been present for four or five years. Except for one area the size of a small pea on the left breast there are no lesions beyond the midline. There are no subjective symptoms. The past history has no bearing on the described condition.

A biopsy specimen was taken from the lesion on the right forearm. The only histologic abnormality appears to be questionably dilated blood vessels.

DISCUSSION

Dr. F. H. Stibbens, Oakland, Calif.: I feel that this condition is a nevus.

Dr. C. J. Lunsford, Oakland, Calif.: I thought it interesting that the condition in this case was completely unilateral.

Multiple Hemorrhagic Sarcoma (Kaposi). Presented by Dr. H. J. Templeton, Oakland, Calif.

M. D., a 72 year old white man of Italian birth, presents extensive, sharply marginated, markedly infiltrated, purplish plaques on the hands, wrists, arms and legs of ten years' duration. His general health has been fair. The results of a complete examination of the blood, of a urinalysis and of a Kline flocculation test were normal. A biopsy showed a fibroblastic structure in the corium with many new and dilated blood vessels.

The clinical picture has not been altered by three doses of unfiltered roentgen rays (80 r each) given at weekly intervals.

DISCUSSION

Dr. Ervin Epstein, Oakland, Calif.: Regarding the dosage of the roentgen rays, it might be interesting to record that a patient with this disease whom I have been treating for several years has failed to respond to doses of as much as 1,000 r given in a single treatment.

Dr. C. J. Lunsford, Oakland, Calif.: On the other hand, I had a patient, a Jewish woman, who responded to roentgen ray treatment. When I saw her last summer all of the lesions had disappeared except one; that lesion had received as much roentgen ray therapy as the others.

Dr. A. E. Ingels: Of course, one should not forget that such lesions often regress spontaneously.

Dr. H. J. Templeton, Oakland, Calif.: I presented this case as a typical instance of Kaposi's sarcoma. The thing that interested me most was the widespread distribution in extensive plaques.

Correspondence

STAPHYLOCOCCIC IMPETIGO CONTAGIOSA

To the Editor:—Dr. Seymour J. White's remarks [1] concerning my paper on staphylococcic impetigo contagiosa [2] revived the discussion of Sabouraud's claim that all impetigo contagiosa is streptococcic in origin. The fact that, as far as I can see, all experimental work on impetigo contagiosa for nearly a generation has disproved Sabouraud's views led me to the belief that this old controversy was only of historical interest. Therefore, I restricted the discussion of this subject in my paper to a few remarks.[3] It would be tempting to show in detail how and why Sabouraud failed and refused to recognize the separate entity of a staphylococcic impetigo contagiosa,[4] but this would exceed the space for a letter. Therefore, I shall discuss only Dr. White's points in the order presented in his letter. I should like to emphasize again that the conception of a staphylococcic type of impetigo contagiosa distinct from the streptococcic form is by no means original with me.[3] Furthermore, I do not believe that any one can admire Sabouraud's work more than I do, as a major part of my experimental endeavors have been devoted to the great master's fields: mycotic and pyodermic infections.

There does not seem to be much difference between Sabouraud's and my description of the original blister of streptococcic impetigo. I wrote:[2] "The original vesicle of streptococcic impetigo is so short lived that usually it is not observed; however, on the fingers, where the horny layer is thicker, larger persisting purulent blisters appear." Sabouraud's [5] description is as follows: "The elementary lesion of the impetigo originally is an erythematous spot giving rise to a small soft vesicle ("une petite vessie molle") which contains a clear and translucent liquid. This second stage also is short lived, at least on the face, because the covering horny membrane is very thin."

Dr. White was correct in stating that Sabouraud has described forms of impetigo which correspond to what now is recognized as staphylococcic impetigo. I had mentioned this fact previously.[6] It is, furthermore, correct that the bullous type of impetigo contagiosa was known to Sabouraud.[7] Sabouraud termed the bullous type "impetigo of Tilbury Fox." Previously [8] he had done exactly the opposite and had identified "impetigo with heavy and discoid crusts," now the

1. White, S. J.: Impetigo, Arch. Dermat. & Syph. **43**:704 (April) 1941.

2. Epstein, S.: Staphylococcic Impetigo Contagiosa, Arch. Dermat. & Syph. **42**:840 (Nov.) 1940.

3. Epstein,[2] pp. 846 and 847.

4. Epstein, S.: Beitrag zur staphylogenen Impetigo contagiosa, Dermat. Ztschr. **70**:328-340, 1935.

5. Sabouraud, R.: Impetigo, in Besnier, E.; Brocq, L., and Jacquet, L.: La pratique dermatologique, Paris, Masson & Cie, 1901, vol. 2, p. 868.

6. Epstein,[2] p. 846 (footnote 13); footnote 4, p. 332.

7. Sabouraud, R.: (*a*) Pyodermites et eczémas, Paris, Masson & Cie, 1928; (*b*) Diagnostic et traitement des affections du cuir chevelu, ibid. 1932.

8. Sabouraud, R.: Etude clinique et bactériologique de l'impétigo, Ann. de dermat. et syph. **1**:62, 320 and 427, 1900.

streptococcic type, as "typical impetigo of Tilbury Fox." Fox's papers,[9] apparently more cited than read, reveal that Fox included both the crusted and the bullous types of impetigo under his name of impetigo contagiosa. This term, therefore, is correctly used only if it covers both varieties.

That Sabouraud failed to recognize the multiple causation of impetigo contagiosa may be partly due to the fact that the streptococcic type predominated in his material, whereas bullous impetigo, as he stated repeatedly,[10] was exceedingly rare. The experience of others who had become familiar with this type of impetigo and who had used bacteriologic methods equal to those employed by Sabouraud apparently failed to impress him. Although the bibliography of his book [7a] contained most of the important modern articles on staphylococcic impetigo,[11] they were all ignored in the text.

Dr. White's quotation that I have never seen streptococcic impetigo turn into staphylococcic impetigo but that I have seen apparently staphylococcic lesions assume the picture of streptococcic impetigo is correct. This is not contrary to the opinion of Sabouraud, as Dr. White believes. I cannot find one instance in which Sabouraud described a bullous impetigo developing on top of the streptococcic type with the yellowish crusts. All that Sabouraud claimed [12] is that in streptococcic impetigo there are frequent secondary infections of staphylococcic folliculitis, a condition which neither Sabouraud nor the proponents of a staphylococcic type of impetigo have considered impetigo contagiosa.[13]

Dr. White's statement that the staphylococcus in impetigo is always a secondary invader and that the streptococcus never takes second place to the staphylococcus and is never a secondary invader of lesions caused by the staphylococcus corresponds with Sabouraud's opinion. However, "Sabouraud's law," as it was called, cannot be upheld in this strict formulation for the following reasons:

1. While it is true that staphylococci are by far more frequently found as secondary invaders than streptococci, it has been definitely proved that streptococci can be found as secondary invaders in staphylococcic infections.[14]

2. The demonstration of streptococci in a cutaneous lesion is no proof of their etiologic role, especially when they are cultured by a procedure as sensitive as the pipet method of Griffon-Balzer, used by Sabourand. Jordan [15] showed that by

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9. Fox, W. T.: On Impetigo Contagiosa or Porrigo, Brit. M. J. **1**:467, 495, 553 and 607, 1864.

10. Sabouraud,[7a] p. 121; footnote 8.

11. Dohi, K., and Dohi, S.: Zur Klinik und Ätiologie der Impetigo contagiosa, Arch. f. Dermat. u. Syph. **111**:629-646, 1912. Fuchs, D.: Beiträge zur Frage der Impetigo und des Ecthyma, ibid. **139**:132-140, 1922. Lewandowsky, F.: Zur Impetigo-Frage, ibid. **138**:438, 1922. Dohi, K., and Kurita: Beiträge zur Lehre von der Impetigo, Jap. J. Dermat. & Urol. **4**:3-4, 1904.

12. Sabouraud.[5] Sabouraud,[7b] p. 42.

13. Epstein,[2] p. 846 (footnote 12).

14. Epstein.[4] Biberstein, H.: Bakteriologische Einleitung zu den Pyodermien, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1934, vol. 9, pt. 2, pp. 1-28. Jessner, M.: Impetigo contagiosa und Ecthyma simplex, ibid. pp. 35-158.

15. Jordan, P.: Über die Häufigkeit des Vorkommens von Streptokokken auf normaler Haut, Arch. f. Dermat. u. Syph. **159**:152, 1929.

means of this method streptococci can be demonstrated in nearly 100 per cent of specimens of normal skin.

Therefore, the bases for Sabouraud's assumption have been proved to be erroneous.

Dr. White put Sabouraud's opinion above facts demonstrated by investigators who studied bacteriologically and experimentally staphylococcic as well as streptococcic impetigo. The opinion of no matter how good a man can never outweigh facts. It does not detract anything from Sabouraud's greatness to admit that the conception that all impetigo contagiosa is streptococcic is erroneous.

Impetigo contagiosa is a common condition. The methods used in those investigations which proved the existence of separate staphylococcic impetigo contagiosa have been published and can be repeated by any one. It might help to settle this controversy for good if investigators who still put Sabouraud's opinion above experimental evidence would undertake a bacteriologic study of the two clinical types of impetigo and publish their findings.

STEPHAN EPSTEIN, M.D., Marshfield, Wis.

Book Reviews

The Chemical Action of Ultraviolet Rays. By Carleton Ellis and Alfred A. Wells. Revised and enlarged edition by Francis F. Heyroth, M.D., Ph.D. Price, $12. Pp. 961, with 159 illustrations. New York: Reinhold Publishing Corporation, 1941.

Dermatologists were the first physicians to popularize ultraviolet ray therapy. The popularity has become so vast that dermatologists no longer rely on this form of therapy in office practice. Patients own ultraviolet emanators and expose themselves, well or ill, to the radiation. Clubs and gymnasiums, swimming pools and barber shops offer their clientele exposure of the skin to ultraviolet radiation. The American Medical Association has taken cognizance of this state of affairs through its Council on Physical Therapy.

Professor Heyroth has brought the Ellis and Wells text of a few years back up to date. This monumental work—compilation, abstract comment, replete with references—is a text of 950 pages. Every aspect of the problem of ultraviolet rays of interest to the chemist, the physiologist and the pathologist is covered. It is an encyclopedia in content yet a handbook in physical dimensions. The fringes have been removed. Only woof and web are given.

Choose the chapter "The Physiologic Effects of Ultraviolet Rays" for study. Very properly, there is the statement: "In the extensive literature many apparent contradictions abound." Then there follow a résumé of the theories of action of ultraviolet rays, statements of possibilities expressed by authorities, graphs of absorption curves for the various layers of skin (largely from Bachem) and a complete résumé of explanations of the mechanism of the production of erythema and pigmentation. A decade past Lucas recognized the difficulties involved in physical measurement.

Dermatologists are interested in sunburn-preventive creams and protective salves. A page or so is devoted to this subject, with mention of the constituents of sunburn preventives and tan stimulants. The physical-acting "parasols," the chemical-acting "parasols" and combinations of the two are included in the discussion of such items as titanium, esculin, menthyl salicylate and many less well known and in some instances patented substances. Manufacturers and purveyors of these preparations must recall the requirements of the national food, drug and cosmetic laws before making claims for their products.

The book carries the reader whose primary interest is industry, research, physics, manufacture of apparatus, air sterilization or any of many other arts and sciences through the entire range of influence of ultraviolet rays in his chosen field. Ellis and Wells have a way of doing just this sort of thing, whether the topic is hydrogenation of fats and oils or ultraviolet rays.

Reinhold continues to do a good job in book making too.

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